NOVEMBER 26, 1955 PAGES 1097 TO 1148

6 14 DEC 1955 Cont. Copy Per. (Sec. 8)

# THE LANCET

*Offices:* 7, ADAM STREET, ADELPHI, W.C.2
Telegrams: LANCET, RAND, LONDON Telephone: TEMPLE BAR 7228 and 7229

No. XXII OF VOL. II, 1955 LONDON, SATURDAY, NOVEMBER 26, 1955 Pp. 112—Price 1s. 6d.
No. 6900 VOL. CCLXIX Founded 1823 PUBLISHED WEEKLY Registered as a Newspaper Annual Subscription: £3 3s.

## 'PERNIVIT' FOR CHILBLAINS

*Tablets containing Acetomenaphthone B.P. and Nicotinic Acid B.P.*

The vasodilator action of nicotinic acid and the effect of vitamin K in maintaining normal vascular permeability and blood coagulability are combined in Pernivit to provide a rational and effective treatment.

Bottles of 50 and 500 tablets.

*Literature and specimen packings are available on request*

THE BRITISH DRUG HOUSES LTD. (Medical Department) LONDON N.1

*Second Edition*

SURGERY: A TEXTBOOK FOR STUDENTS

By CHARLES AUBREY PANNETT, B.Sc., M.D., F.R.C.S. Professor of Surgery, University of London; Director of the Surgical Unit, St. Mary's Hospital, London; sometime member of the Court of Examiners, R.C.S. Eng., and Examiner to the Universities of London, Manchester, and Cardiff.

769 + xiv Price 27s. 6d. net, plus 1s. postage
Extensively illustrated throughout the text.

The book has been completely revised to incorporate advances in surgery since the issue of the first edition. At the same time unnecessary matter has been avoided, so that the book remains a presentation of modern surgery of moderate size. The character of the book has been preserved but the additional matter makes it more generally useful to postgraduate as well as undergraduate students.

Hodder & Stoughton Ltd., 20, Warwick-square, London, E.C.4

*Second Edition*

THE CARE OF TUBERCULOSIS IN THE HOME

By JAMES MAXWELL, M.D., F.R.C.P. Physician, Royal Chest Hospital; Physician to the Ministry's Mass X-ray Unit; Consulting Physician, Royal National Sanatorium, Bournemouth; late Physician, St. Bartholomew's Hospital

Demy 8vo 114 + xii Illustrations 7s. 6d. net, plus 4d. postage
Hodder & Stoughton Ltd., 20, Warwick-square, London, E.C.4

HOW TO WORK—
ADVICE TO STUDENTS STARTING MEDICINE.

An address to the London Hospital Medical Society.
By A. E. CLARK-KENNEDY, M.D. Camb., F.R.C.P.

Demy 8vo. 16 pages. Price 1s.
The Lancet Limited, 7, Adam-street, Adelphi, London, W.C.2

BRITISH OBSTETRIC AND GYNÆCOLOGICAL PRACTICE

Edited by Sir EARDLEY HOLLAND, M.D., F.R.C.S., F.R.C.O.G., and ALECK BOURNE, M.A., M.B., F.R.C.S., F.R.C.O.G.

*In two volumes, sold separately:*

| | | | |
|---|---|---|---|
| OBSTETRICS | 1164 pages | 400 illustrations | 115s. net |
| GYNÆCOLOGY | 850 pages | 370 illustrations | 95s. net |

Prospectus available
Wm. Heinemann Medical Books Ltd., Gt. Russell-street, W.C.1

DISABILITIES
AND HOW TO LIVE WITH THEM
by 55 Patients

Demy 8vo 252 pages Price 10s. 6d. net, plus 6d. postage

". . . it ought, we believe, to be made the compulsory reading of every medical student. It would enrich his humanity and add immensely to his subsequent value as a doctor."—*Medical Press.*

The Lancet Limited, 7, Adam-street, Adelphi, London, W.C.2

THE LAW AND ETHICS OF DENTAL PRACTICE

By R. W. DURAND, M.R.C.S., L.R.C.P.
Formerly Secretary of the Medical Protection Society
and
D. MORGAN, L.D.S. Leeds)
Formerly Deputy Dental Secretary of the British Dental Association

Foreword by Professor R. V. BRADLAW, M.D.S. Dunelm, F.D.S., M.R.C.S. Eng.
Professor of Oral Pathology, Durham University
Director, Newcastle-upon-Tyne Dental School

Expert guidance on the many problems which confront the dentist

Demy 8vo 98 + viii Price 7s. 6d. net, plus 4d. postage
Hodder & Stoughton Ltd., 20, Warwick-square, London, E.C.4

*EDWARD ARNOLD*

*Monographs of the Physiological Society*

**No. 3 Neural Control of the Pituitary Gland**

By G. W. HARRIS, F.R.S., Sc.D., M.D.

Ready 1st December.

308 *pages.* 54 *illustrations.* **30s.** *net.*

**No. 2 Man in a Cold Environment**

By A. C. BURTON, Ph.D., and O. G. EDHOLM, M.B., B.S.

An evaluation of the physical and physiological problems of man in the cold. **30s.** *net.*

**Modern Public Health for Medical Students**

By I. G. DAVIES, M.D., F.R.C.P., D.P.H.

Ready 8th December. 496 *pages.* 62 *illustrations.* **30s.** *net.*

41 *MADDOX STREET, LONDON, W.1.*

# CŒLIAC DISEASE *

WILFRID SHELDON
C.V.O., M.D Lond., F.R.C.P.
PHYSICIAN FOR DISEASES OF CHILDREN, KING'S COLLEGE HOSPITAL, LONDON; PHYSICIAN TO THE HOSPITAL FOR SICK CHILDREN, GREAT ORMOND STREET, LONDON

THE three Lumleian lectures delivered by my old teacher Sir Frederic Still (1918), together with the Rachford lectures delivered by Sir Leonard Parsons (1932), constitute perhaps the two most important British dissertations on cœliac disease in the first half of this century. I shall mainly concern myself with continuing the story to the present day. To do so, I shall draw on the records of 74 children with cœliac disease who have been admitted to my wards since 1947. For so large a number I am deeply indebted to my colleagues at Great Ormond Street, who for five years allowed all the cases to come under my care, and later gave me sanction to treat, in a special outpatient clinic, an additional 40 cases that had previously been in their charge.

## Diagnosis

Cœliac disease today remains one of a dwindling group of ailments that have to be recognised on purely clinical grounds, for there is no laboratory test to give the diagnosis the stamp of certainty. Perhaps this makes the disease all the more piquant and challenging. The diagnosis rests on the views of the clinician as to what constitutes the disease. To keep a correct perspective one cannot do better than refer to Gee's (1888) original description, in which he gave pride of place to the passage of loose bulky pale offensive motions, and added wasting, muscular atony, anæmia, abdominal distension, and cessation of growth. These symptoms remain today the hallmarks of cœliac disease.

Still noted that the liver is often so small as to be impalpable; and although this observation has received scant attention it is important to the clinician because it offers a possible point of distinction from chronic intolerance of starch. In 28 of 60 cases in which I have records of the size of the liver at the time of admission it could not be felt at all, and in another 12 it was palpable only high in the xiphisternal notch.

It is, too, of some historical interest that, in referring to the cessation of growth, Still was the first to remark on the younger bone age judged by the skiagraphic appearance of the ossific centres.

Fourteen years later Parsons (1932), in describing the blood chemistry and fat-balances, recorded the impact of biochemical investigation on our knowledge of cœliac disease.

The most noteworthy advance since then has concerned treatment, which in turn has altered the prognosis, and it is these two aspects that I deal with here.

## Treatment

### *Intake of Fat*

Children with cœliac disease always show great difficulty in tolerating both starchy food and fat, and restriction of one or other or both in the diet has characterised the various treatments.

Although protein is well tolerated, Macrae and Morris (1931), Andersen (1947), and Frazer (1952), on the grounds of increased excretion of nitrogen, defective absorption of urea, and hypoproteinæmia in the face of a therapeutic response to high-protein diet, have intimated that a defect in protein metabolism also exists.

The looseness of the motions, the gaseous abdominal distension, and the ease with which diarrhœa can be provoked when complex carbohydrates are added to the diet have led to treatments in which restriction of starches has been held to be of primary importance. Dr. Christian Herter was the pioneer of this approach, and his pupil Dr. John Howland (1921) stated that "carbohydrate is the one which must be rigorously excluded; that with this greatly reduced the other elements are almost always well digested even though the absorption of fat may not be so satisfactory as in health." Howland's fellow pupil, Dr. Sidney Haas, restricts carbohydrates to those contained in fruits, vegetables, and protein milk, and it was he who demonstrated (Haas 1924) the value of ripe banana, which has since been so prominent in treatment. Fanconi (1928) recommended a closely comparable diet.

Meanwhile in this country Still and Parsons regarded the withholding of fat as of primary importance, although the difficulty with starches was recognised and their avoidance at the beginning of treatment was advised. Still observed that bread was particularly badly tolerated. To describe the lot of the child with cœliac disease under these conditions I cannot do better than quote from Still's lecture:

> "Wasted and feeble, the child passes an invalid existence with intervals of improvement followed by a relapse, until, as a result of rigorous dieting, the stools gradually become more normal, and the child eventually struggles back to health, able to take food more or less like other people, but handicapped in growth by the lost time during which the development has been arrested. Even such a favourable result, however, is not to be expected in all cases, for the relapses with increased looseness of the bowels are exhausting, and may end fatally."

One cannot fail to note the importance that was attached to the quality of the stools; indeed for many years the reduction of fæcal fat that followed removal of fat from the diet, which was, of course, an inevitable consequence, was regarded with much solace. Looking back to that period we get a strong impression that the treatment of the stools bedevilled the treatment of the child. Miller must have had this in mind when he wrote:

> "It is unwise perpetually to starve the patient of fat, treating the stools and not the child. . . . In active stages of the disease, however, the fat in the diet should be reduced" (Miller et al. 1920).

In the early days of fat-balances Macrae and Morris (1931) showed that an increased intake of fat by children with cœliac disease led to an increased absorption, and Parsons (1932) stated that fat-absorption could be as high as 83% in spite of a high output of fat in the stools. Yet the significance of this seems to have been overlooked, for he maintained his objection to dietary fat, thus depriving the child of the opportunity of absorbing four-fifths of it.

Although fat-balances in young children with cœliac disease will always present a heavy nursing problem, the technique devised by van de Kamer et al. (1949) of using wet stools and expressing the result as a series of three-day sliding means has gone far to ease the difficulties, and their use has done much to place our new knowledge on a firm basis.

When one recalls Still's description of the outlook for children with cœliac disease, the sense of ineffectiveness when faced with their care can be imagined. Was the withholding of fat really necessary, or might the mismanagement of fat possibly be secondary to intolerance to starches? With the aid of fat-balances this was put to the test by giving a diet that contained unrestricted fat but in which starches were either given or entirely withheld. The result of this experiment, which has already been published (Sheldon 1949), showed that, when starchy foods were withheld, fat-absorption increased significantly. An unexpected and incidental finding was that the children receiving a normal fat-intake without starches improved almost fantastically and were

* The Charles West lecture delivered before the Royal College of Physicians of London on Nov. 15, 1955.

TABLE I—CALORIES NEEDED TO ENABLE CŒLIAC CHILDREN TO GROW

| Age (yr.) | Calorie intake per lb. of | | No. of cases |
|---|---|---|---|
| | Actual weight | Expected weight | |
| 1–2 | 62–122 | 45–79 | 18 |
| 2–3 | 57–90 | 40–52 | 6 |
| 3–5 | 45–76 | 34–56 | 13 |
| 5–7 | 38–90 | 27–51 | 6 |
| 7–12 | 38–67 | 22–38 | 6 |

quickly made happy and active. At last the régime of rigorously excluding fat appeared to be doomed.

A year later evidence came from Holland that the deleterious factor in starchy foods was contained in the protein fraction of wheat and rye flour, but before elaborating this I ought to mention three other lessons that arose from our investigations.

In the first place there was no reliable correlation between the amount of fat absorbed and the amount in the dried stool, a conclusion that had already been reached by Cooke et al. (1946); hence in previous years it had been undoubtedly fallacious to allow the figure for fæcal fat to dominate treatment. French (1955) expressed the situation well when he said that estimations of fæcal fat should be abandoned as evidence of steatorrhœa, both in diagnosis and in charting recovery.

Secondly, if a wasted child is to thrive, it is not enough simply to provide a diet of correct quality; quantity, measured by the calorie value, must also receive close attention. This is a situation to which pædiatricians are already accustomed when striving to nourish an infant after a prolonged attack of gastro-enteritis and when advising on the feeding of healthy infants. The calorie intake of children with cœliac disease on the old low-fat régime received but little attention, probably because appetite remained so feeble that a target in terms of calories was out of the question. The position today is different, for on a modern diet these children soon develop a good appetite. Table I shows the calorie intake that we found necessary to enable children with cœliac disease to grow. In general, the greater the degree of emaciation the higher must be the initial calorie intake, and almost always it needs to be higher than would be accorded a healthy child.

The third point arises from the second. A diet without any starchy foods reduces the variety of the menu, and in consequence a few of the children did not attain a high enough calorie intake to enable them to gain weight. This was overcome by augmenting the diet with glucose and steadily increasing the amount until the critical calorie level was reached, at which point the weight began sharply to rise. This is shown by fig. 1, which refers to a girl, aged 5 years, who had had cœliac disease since the age of 15 months. Glucose was added daily to her starch-free diet, but it was not until her calorie intake had been worked up from 72 to 90 calories per lb. of body-weight, and the daily allowance of glucose had reached 5 oz. that her weight steadily increased. Fig. 1 shows the general point that weight gain in wasted children depends mainly on an adequate calorie intake. It also illustrates how well children with cœliac disease tolerate and utilise glucose, a feature also noted by Andersen and di Sant' Agnese (1953). To my mind this must throw some doubt on the widely held view that the flat blood-sugar curve, so common in cœliac disease, is due to defective absorption of glucose.

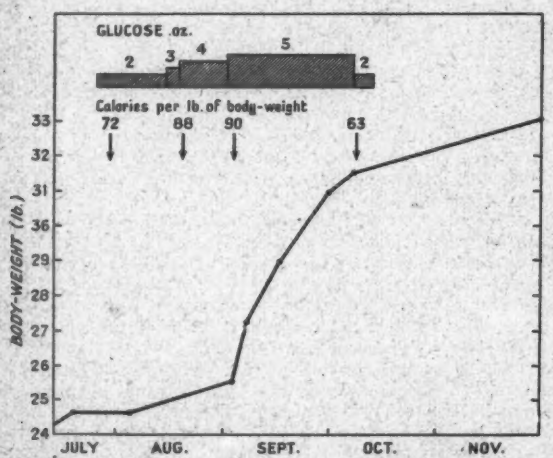



Fig. 1—Use of glucose to achieve caloric intake needed to enable a child, aged 5 years, with cœliac disease to grow normally on starch-free diet.

*Gluten*

Reference has already been made to the work from Holland:

Dicke (1950) claimed that the substance injurious to children with cœliac disease was contained in wheat and rye flour, but wheat starch—i.e., wheat flour from which the protein fraction called gluten has been removed—was harmless.

Weijers and van de Kamer (1950) showed that the adverse effect of wheat flour lay in increasing the excretion of saturated rather than unsaturated fatty acid, and they considered that some of the excreted fat had been mobilised from the body's fat-depots.

TABLE II—ADVERSE EFFECT OF GLUTEN ON ABSORPTION OF FAT

| Case no. | Age | | Duration of cœliac disease | | Fat-absorption (%) on wheat-starch diet | |
|---|---|---|---|---|---|---|
| | (yr. | mos.) | (yr. | mos.) | Without gluten | With gluten |
| 1 | 2 | 3 | 1 | 2 | 91 | 81 |
| 2 | 10 | 5 | 9 | 0 | 89 | 87 |
| 3 | 7 | 0 | 4 | 6 | 93 | 89 |
| 4 | 4 | 2 | | 3 | 92 | 78 |
| 5 | 3 | 2 | 1 | 2 | 92 | 87 |

Though opinion on the question of active fat-excretion into the bowel remains divided, the harmful effect of wheat protein in cœliac disease has been confirmed in several countries:

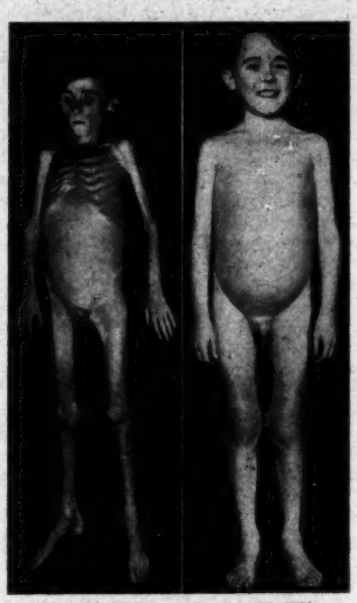
Frazer and his colleagues (Anderson et al. 1952) in Birmingham showed conclusively the evil influence of gluten on fat-absorption and added that this was irrespective of agenisation. At Great Ormond Street confirmation was obtained in 5 cases (table II).

Even more striking was the havoc wrought to health by the addition of gluten, which was in some children great enough to render fat-balances impracticable. Confirmation has also come from Ragazzini et al. (1953) in Italy, Grette and Imerslund (1953) in Norway, and Krainick and Debatin (1954) in Germany.

The dramatic response that is sometimes seen when a diet simply devoid of gluten is given to a grossly wasted child with cœliac disease is well illustrated in the photographs of a boy, aged 10 years, treated in this way by my colleague Prof. A. A. Moncrieff, to whom I am indebted for the case. The photographs (fig. 2) were taken at an interval of only two months, the speed of improvement being quite remarkable; indeed further comment on the benefit of withholding gluten seems almost superfluous.

Gluten contains two proteins, gliadin and glutenin, which possess different solubilities in alcohol, and attempts have been made to decide which one is responsible for the untoward effect of gluten. van de Kamer et al. (1953) concluded that the harmful action must mainly be sought in the gliadin fraction. We have fed

both components to 7 cœliac children, giving 5 g. daily to the younger children and 10 g. daily to those aged more than 5 years, but the results have not been at all decisive. Glutenin was harmful and lowered fat-absorption in 3 children, and in 4 others gliadin exerted a like effect. The difficulty, however, of obtaining either protein free from contamination by the other may have contributed to such equivocal results.



Nov. 21, 1951 Jan. 25, 1952

**Fig. 2—Remarkable improvement on two months' gluten-free diet in a boy, aged 10 years, with severe cœliac disease.**

The proteins of oat flour include a gliadin, which is reputed to contain a higher cystine content than does wheat gliadin, and a glutelin, and Dicke et al. (1953) suggest that oat flour is injurious to children with cœliac disease. If this proves correct, the diet must be modified accordingly; but in my experience the children seem to tolerate oat flour satisfactorily, except those who dislike its taste. To investigate this point more closely the fat-balances of 6 children with cœliac disease were determined (table III). Two ounces of oat flour daily was probably too much for the sixth child, making her slow over her meals and slightly increasing the number of her stools, but otherwise oat flour appeared to have no untoward clinical effect. If a child likes it, we allow it in the diet.

Thus the objective today in treatment is to give a diet which strictly avoids gluten but is in all other respects normal. The diet therefore includes flours other than those of wheat and rye. Wheat starch, because it has proved harmless, is given, and with the use of special recipes it can be made into bread, cakes, and biscuits. The details of such a diet have been fully described elsewhere (Sheldon and Lawson 1952, Sheldon 1954) and need not be described again here. Vitamin supplements of A, B complex, C, and D should be given.

Although most children with cœliac disease can be transferred quickly and easily to a standard gluten-free diet, in a few the illness may have already become so severe that a probationary period on a much simpler diet—e.g., skimmed milk, 'Prosol,' glucose, and banana purée—may be required, and a month or more of skilful nursing may be needed before a full gluten-free diet can be tolerated. For the child who presents with œdema and perhaps ascites associated with hypoproteinæmia one or more transfusions of plasma may be necessary, as in 3 of my 74 cases. Of complications other than œdema, tetany deserves the greatest respect, and intramuscular calcium should be supplied until the serum-calcium level has been restored to normal.

TABLE III—EFFECT OF OAT FLOUR ON ABSORPTION OF FAT

| Case no. | Age (yr.) | Age (mos.) | Duration of cœliac disease (yr.) | Duration of cœliac disease (mos.) | Fat-absorption (%) (8-day balances) on gluten-free diet: Without oat flour | Fat-absorption (%) (8-day balances) on gluten-free diet: With oat flour | No. of days before balance | Oat flour (oz. daily) |
|---|---|---|---|---|---|---|---|---|
| 6 | 4 | 3 | 3 | 10 | 95·5 | 97 | 7 | 2 |
| 7 | 1 | 9 | | 4 | .. | 93 | 10 | 1 |
| 8 | 5 | 10 | 4 | 10 | 87·0 | 87 | 14 | 1 |
| 9 | 7 | 2 | 4 | 8 | 93·0 | 93 | 26 | 1 |
| 10 | 10 | 4 | 9 | 4 | 91·0 | 89 | 14 | 2 |
| 11 | 4 | 2 | 3 | 2 | 91·0 | 88 | 7 | 2 |

*Anæmia*

Success can also be deferred if anæmia is overlooked. Broadly speaking, I have relied on medicinal iron when the hæmoglobin has been above 65%; but, when it has been below that figure, one or more blood-transfusions have been given. The more rapid recovery from anæmia which transfusion offers not only speeds the well-being of the child, including appetite, but also quickly increases resistance against infection and facilitates recovery should infections arise. My impression is that the value of blood-transfusion in these children is not sufficiently realised; of the 74 cases admitted to my wards, transfusion of blood was thought necessary in 18 (24%).

## Prognosis

What has been the impact of the new dietary treatment on prognosis? Hardwick (1939) found a mortality of 15% in 544 published cases, but today cœliac disease has virtually ceased to be fatal. Earlier workers emphasised that survival was often obtained at the cost of stunting of growth, which is of course a matter of height rather than weight, and that care with the diet might be necessary for years. In the words of Sir James Goodhart, these children were made "safe but not sound."

With mortality virtually annihilated, more stringent criteria must now be applied to distinguish between survival and cure, and for the child merely to arrive at a modus vivendi should not continue to be regarded with complacency. The important contribution by Bennett et al. (1932) revealed how cœliac disease might linger into the idiopathic steatorrhœa of adults, and Cooke et al. (1953) found that of 100 adults 43 had had an onset in childhood. As regards the effect of a gluten-free diet in idiopathic steatorrhœa of adults, all one can say is that the published results appear to have been very variable, and one may wonder whether, with time, the condition can become irreversible, although French (1955) points out that recovery may take much longer in the adult than in the child, and he suggests that failure with a gluten-free diet may be because the treatment has been abandoned too soon.

Frazer (1952) has pointed out that exclusion of gluten leads to a reduction in fæcal fat, a return towards normal of the radiographic appearance of the small intestine, and a gradual improvement in the chylomicron count and the glucose-tolerance test. When, however, Gerrard et al. (1955a) reinvestigated 32 children treated by the older methods, not one was found completely free from symptoms. There was, too, an over-all significant reduction in height and weight below normal, and only 6 showed a normal glucose-tolerance curve. Survival, rather than cure, seems a fitting description for these children.

Whether a normal glucose-tolerance curve should be insisted on before speaking of cure is difficult to decide. At Great Ormond Street we repeated the glucose-tolerance tests on 30 children with cœliac disease. 4 had had their disease for six years or more and had never received a gluten-free diet; 3 of these showed flat curves—i.e., an increase of less than 40 mg. of blood-sugar per 100 ml. Of the remaining 26 children, with a duration of disease from two and a half to eleven years, all had undergone a period of gluten-free treatment, but at the time of the test all had been returned to a normal diet; 17 of them still had a flat curve. The children had been admitted to hospital in the evening and their glucose test done next

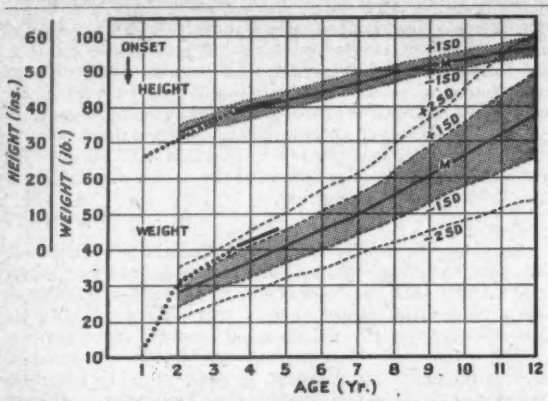



Fig. 3—Growth of child with cœliac disease which came on at the age of 7 months: after 2½ years on gluten-free diet (interrupted lines) height and weight were above average and were maintained thus during the next year on gluten-containing diet (solid lines).

morning, and in view of the high proportion of flat curves we wondered whether psychological influences due to the test being done so promptly after admission could have affected the results. However, 13 control children, carefully selected to avoid any with pyrexia, recent infection, or metabolic disorder, were examined in precisely the same way, and 10 of them showed a normal rise in the blood-sugar level.

It would be interesting to know whether healthy adults who give a history of cœliac disease in childhood have a normal glucose tolerance; until such information is available it may be unwise to demand a normal glucose tolerance as a criterion of recovery. Certainly the conclusion reached by Cooke et al. (1953), that in idiopathic steatorrhœa of adults there is no correlation between glucose tolerance and the clinical state, seems equally applicable to cœliac disease.

*Growth*

An important aspect of prognosis concerns growth, for a legacy of stunting cannot be regarded as a satisfactory outcome. Even if early cases grow normally when on a gluten-free diet, while in late cases growth is accelerated, as Gerrard et al. (1955a) have shown, the question of how long such treatment must be continued to ensure that normal growth shall continue after reversion to a normal diet calls for an answer.

Both Hardwick (1939) and Gerrard et al. (1955b) have recorded the average deviation below standard height and weight in groups of children with long-standing cœliac disease, but although their figures have statistical significance they afford little help when an individual is studied, for some children are inherently tall and some are short. One really needs to be able to compare the height and weight of each child against his personal expected measurements. This is being studied at the hospital founded by Dr. Charles West, where a separate growth chart devised by Dr. Lawson is used for each child with cœliac disease. The chart shows the mean height and weight from 1 to 12 years, and also one standard deviation for height and two standard deviations for weight. During treatment on a gluten-free diet, in the first six months weight is usually gained rapidly, and height increases above average rate, but thereafter each child tends to flatten out into his personal channel of standard deviation, and subsequently his movement into a higher or lower channel can be followed and the influence of changes of diet be recorded.

Figs. 3–7 illustrate some of our findings. On the charts the interrupted line represents a gluten-free diet and the subsequent solid line a diet containing gluten.

The charts of 114 children have been analysed. The method adopted has been to express increments of height and weight as a percentage of the mean increments over the same time. The figure of 100% implies that growth is exactly keeping pace with the mean rate of growth.

The results of the analysis are shown in fig. 8. On a diet without gluten, after the initial spurt in growth during the first six months, both height and weight continued to increase at a rate above the average until gluten was restored to the diet, whereupon the increments in height and weight fell away. In several children the interference with growth was sufficient to make us reinstitute a period on a gluten-free diet, when once again growth accelerated. This second period varied from four months to three years; yet, when for a second time gluten was reintroduced, the rate of growth in two-thirds of the children again dropped below the average.

It has been suggested that a gluten-free diet ought to be maintained throughout the years of growth, but our findings are not quite in accord with this, because some children with cœliac disease, after a period on a gluten-free diet, continue to grow satisfactorily when gluten has been reintroduced. The difficulty lies in detecting those children who will behave in this way.

Of the children whom we replaced on a gluten-free diet, in a few the reason lay in a return of symptoms of cœliac disease when they had been given gluten, but in the majority the sole reason was that growth had checked, there has been no other clinical evidence of relapse, and the falling off in the rate of growth, especially height, would have been easily overlooked without the regular charting of the growth record.

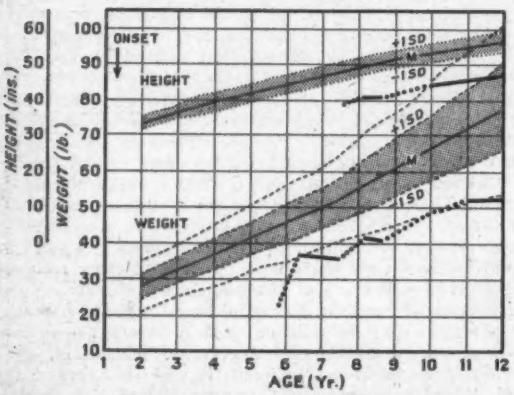



Fig. 4—Growth of child with cœliac disease which came on at the age of 16 months: repeated introduction of gluten-containing diet (solid lines) led to cessation of growth.

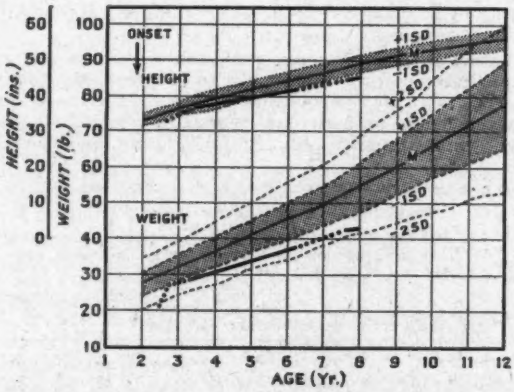



Fig. 5—Growth of inherently small child with cœliac disease which came on at the age of 1 year 11 months: a second period on gluten-free diet (interrupted lines) did not accelerate growth.

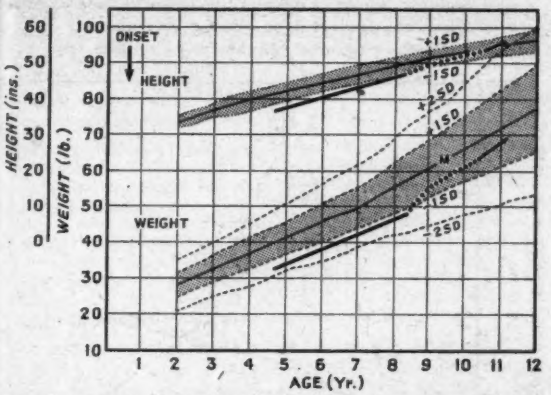



Fig. 6—Growth of child with cœliac disease which came on at the age of 7 months: first solid lines show growth on gluten-containing fat-free diet for more than 3 years, whereas 2 years on gluten-free diet (interrupted lines) was accompanied by accelerated growth.

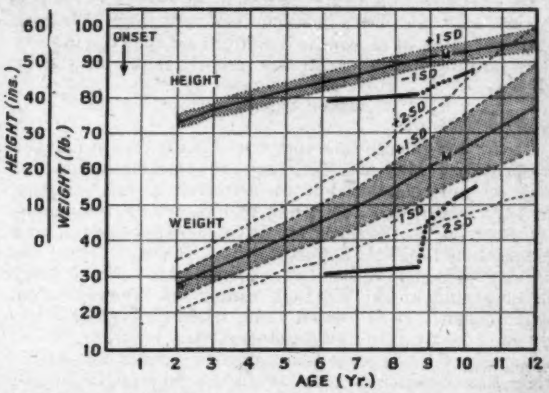



Fig. 7—Growth of child with cœliac disease which came on at the age of 6 months: first solid lines show growth on gluten-containing fat-free diet; gluten-free diet (interrupted lines) led to a spurt in growth, but disastrous effect of early treatment on growth was probably too great to enable him to make up for lost ground.

If therefore a return to a normal diet is to be attempted during childhood, and if at the same time satisfactory growth is to be achieved, it appears essential to keep a close watch on the height and weight gradients, comparing these with the gradients while the child was receiving a gluten-free diet, so that if growth definitely falls off it may be started again by restoring the special diet before too much has been lost.

### Action of Gluten

The mechanism by which gluten exerts its harmful influence is not understood. The fact that it operates in this way in so few children suggests that other conditions may first of all have to be satisfied, but we do not know what these may be. Of my 74 patients 9 began to have symptoms while away from home in a residential institution, but whether this indicates a psychological factor or whether epidemic gastro-enteritis was the starting-point, I cannot tell. Ebbs et al. (1950) and Andersen and di Sant' Agnese (1953) consider that the relations of children with cœliac disease show a sufficient incidence of the disease and of diabetes mellitus to point to an underlying hereditary trait.

Frazer (1953) suggests that there may be an allergic reaction to gluten in the small intestine, leading to increased secretion of mucus, which Frazer et al. (1949) have shown to be the cause of the deficiency pattern seen radiologically after a meal of barium, and that excess of mucus may account for delay in absorption. But if there is an allergic factor it can be only a local affair, for van de Kamer et al. (1953) obtained negative skin tests with glutenin and gliadin, and in several children that we have skin-tested with gluten by both scratch and intradermal techniques the results have been uniformly negative.

In some children cœliac disease dates from acute gastro-enteritis, which may in some way disturb the physicochemical conditions in the intestine and thus prepare the ground for cœliac disease. Attempts to isolate pathogenic bacteria from the stools have usually proved fruitless, and it seems that if the intestinal flora plays a part it is through the medium of saprophytes. An attempt was made in 3 children to modify the intestinal flora with aureomycin, which so noticeably lessens the odour of the stools in pancreatic fibrosis. It was given for periods up to six weeks at a time when the diet contained gluten. The results were disappointing: though the average fat-absorption was not appreciably affected, the stools worsened, appetite was lost, and the weight steadily fell. Afterwards each child responded as soon as gluten was withheld.

That cœliac disease is never observed in a baby that is being breast-fed is understandable because the diet is then free from gluten; but, although cœliac disease may appear as soon as gluten is introduced into the diet, the onset may be deferred for a year or more beyond this point; indeed it is conceivable that gluten intolerance does not arise until cœliac disease has already developed.

We do not know whether cœliac disease is ever met with in children who have never had gluten; but, if gluten intolerance is an essential, cœliac disease should only be found in those parts of the world where gluten is eaten. I am grateful to Dr. W. R. Aykroyd, director of the nutrition division of the Food and Agriculture Organisation of the United Nations, for supplying me with figures showing the consumption of wheat in different countries. Inquiries were then sent to doctors interested in nutrition and pædiatrics in several tropical countries.

Cœliac disease is met with in Colombia, Costa Rica, and Mexico, where wheat forms part of the diet. It does not occur or else is not recognised in Senegal, the Belgian Congo, Uganda, Kenya, Eritrea, South India, Malaya, Thailand, Formosa, the Phillipines, the Celibes, Sangir, and Fiji, except for an occasional case in a European child, and in these countries if wheat is eaten at all it is only by Europeans and families of a high-income group.

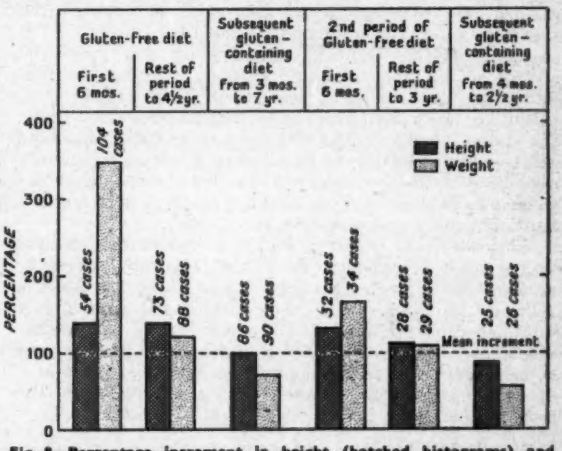



Fig. 8—Percentage increment in height (hatched histograms) and weight (stippled histograms) of children with cœliac disease on gluten-free diet and on gluten-containing diet.

I am of course well aware that medical records in Central Africa and the Far East do not approach Western standards, but at all events it can be said that the inquiry does nothing to undermine the important rôle played by gluten.

## Other Questions

*Glucose Tolerance*

Is the flat glucose-tolerance curve really due to delayed absorption? May and McCreary (1940) thought that this was so and attributed it to defective gastro-intestinal motility. However, by using techniques devised for us by Prof. A. L. Frazer, we have shown (Sheldon and MacMahon 1951) that glucose leaves the stomach of the child with cœliac disease at a normal rate; hence delay in emptying of the stomach cannot be invoked as an explanation. It is known that, when glucose is introduced directly into the duodenum, the resulting blood-sugar curve tends to be flat, suggesting defective absorption, but there is no doubt about the therapeutic benefit of glucose. Emery (1947) has suggested that the flat curve is due to avidity of the liver for glucose, and in this connection the unusually small liver in many of these children may have some significance. Though most workers incline to delayed absorption as the explanation, this is not finally proved.

*Phosphorylation*

Since phosphorylation plays a part in the absorption of fats and glucose, a defect in this mechanism might be of significance, but there is no good evidence that such a defect exists. Morris and Peden (1937) and Hardwick (1939) have reported that the serum-alkaline phosphatase level, in the absence of cœliac rickets, tends to be low, and they attribute this to cessation of growth, which seems likely enough. The serum-alkaline phosphatase level has been estimated for me in 17 older and growing cœliac children, aged 3–9 years, and found to be within the normal range, the figures being 12–28 King-Armstrong units. Fisher and Neill (1955) call attention to the intermittent presence of phosphorylethanolamine in the urine of some children with cœliac disease and their relations. Since this substance acts as a substrate for phosphatase, its presence in abnormal amounts might suggest either a low production of phosphatase or a limitation of its enzyme action. Dr. L. I. Woolf searched for it in the urine of 8 of my patients and found it in all, but he regarded the amount as above normal in only 1. Thus what evidence there is indicates that phosphorylation should be judged not guilty.

*Vitamin B*

Deficiency of vitamin B as a causal factor of cœliac disease has been suggested. May et al. (1942) reported that intramuscular therapy with crude liver and vitamin-B complex led to clinical improvement and improved absorption of vitamin A and glucose. During the next few years the treatment was given a wide trial; but, in spite of a few favourable reports (Paterson et al. 1944), the daily injections into the tissues of these thin and unhappy children proved so irksome that it was generally abandoned. More recently it has been stated that the worst effects of wheat flour could be checked with nicotinamide (Weijers and van de Kamer 1950).

The occasional occurrence of a megaloblastic anæmia that quickly responds to folic acid further involves the vitamin-B complex. This type of anæmia was present in 7 of my 74 cases. Until, however, it has been firmly established that vitamin B will allow a child with cœliac disease to tolerate a completely normal diet and to grow at his expected rate, it seems wiser to regard vitamin-B deficiency as a secondary phenomenon, although none the less one that must be provided for in treatment.

*Intolerance of Starch*

Although there has been general confirmation of the finding of Farber et al. (1943) that children with cœliac disease produce the three pancreatic enzymes in normal amount, Andersen (1947) finds that the amount of amylase is often reduced, but her conception of cœliac disease would not receive general acceptance in this country, for to her steatorrhœa is not an essential symptom, and cœliac disease and intolerance towards starch appear to be synonymous terms to her. There are, however, clinical distinctions, for though starch intolerance could be expected to cause fermentative diarrhœa, abdominal distension, and loss of weight, it would be unlikely to cause steatorrhœa, a small liver, a flat glucose curve, or intolerance to gluten. The following case may serve as an illustration:

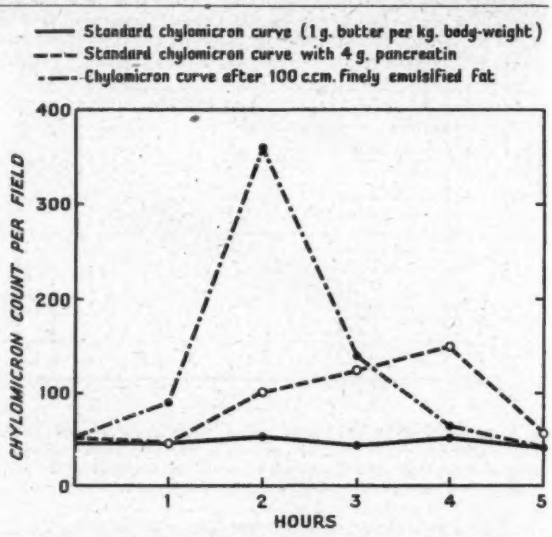



Fig. 9—Chylomicron curves from a boy, aged 2 years, who had no pancreatic lipase.

A boy progressed well until starch was introduced into his diet at the age of 4 months, whereupon his stools became loose, frequent, and undigested but not pale, he ceased to gain weight, and his abdomen became distended. On admission to hospital two months later, in addition to the previous symptoms, his liver was easily palpable and his glucose tolerance was normal. He improved and gained weight as soon as starch was forbidden, and two months later he was able to tolerate small amounts of wheat, rice, and potato. A fortnight later 8 g. of gluten was added daily to his diet and continued for a month without harmful effect, and at the end of this period his fat-absorption was 95%.

To say that he was an early case of cœliac disease, and that the withholding of starch, and therefore of gluten, for two months led to cure would only be permissible if steatorrhœa is regarded as unessential to the diagnosis, and this would not conform to the disease which Gee described.

*Steatorrhœa*

Even if steatorrhœa is held to be an essential feature, it remains but a symptom and may arise from other causes. The most important of these is pancreatic fibrosis, which is seldom difficult to distinguish, for the history is different, and there are laboratory means by which the diagnosis may be confirmed. Simple intolerance of fat with consequent steatorrhœa is also met with, particularly in infancy and after gastro-enteritis, but it responds to curtailment of dietary fat. Frazer and his colleagues have described one such case, and another in which persistent steatorrhœa from the age of 2 months was unrelated to gluten but relieved by bile salts (Ross et al. 1955).

In 2 of my patients also steatorrhœa bore no relation to gluten.

A boy, aged 10 years, had had recurrent symptoms of ulcerative colitis for five years, eventually complicated by cirrhosis of the liver. His fat-absorption was as low as 54%, but under the influence of 1 g. of bile salts daily his absorption rose in a month to 83%.

The other child illustrates a selective absence of pancreatic lipase.

From birth his stools were greasy, with oil droplets separating on the surface. When first seen at the age of 2 years, and again at 5 years, his duodenal juice contained trypsin and amylase but no lipase. His chylomicron curve was completely flat. Professor Frazer kindly supplied us with a solution of fat in a fine emulsion, and when this was given into the duodenum, the chylomicron curve showed a rise of 315 chylomicrons in two hours. The effect of pancreatin was less striking—90 chylomicrons (fig. 9). The boy has remained on pancreatin and continues to grow at a normal rate.

So far as I am aware, this case is unique, although Lowe and May (1951) have recorded a child in whom trypsin alone of the pancreatic enzymes was missing, and another in whom only amylase was absent.

### Conclusions

Many children with cœliac disease are strikingly intolerant of gluten. Whether this is true of all is perhaps as much a matter calling for clarification of terminology as it is for scientific inquiry. Intolerance purely towards either starch or fat should not be confused with cœliac disease. Starch indigestion is most likely to cause difficulty in differential diagnosis, and it is here that, so it seems to me, the introduction from America of the term "cœliac syndrome" has added nothing but confusion.

Frazer and his colleagues (Ross et al. 1955) feel the time has come to separate off a group of patients with cœliac disease and to call their disease "gluten-induced cœliac disease;" and I think the cause of clarity would be served by some such title. Since gluten, however, has not yet been shown strictly to induce cœliac disease, although intolerance to gluten is undoubted, the more simple term "gluten intolerance" is perhaps a better description.

The lot of the child with cœliac disease is decidedly happier than when Still gave his Lumleian lectures, but this is no time for complacency, for there remains much that we do not understand.

### REFERENCES


Andersen, D. H. (1947) *J. Pediat.* **30**, 564.
— di Sant' Agnese, P. A. (1953) *Pædiatrics*, **11**, 207.
Anderson, C. M., Frazer, A. C., French, J. M., Gerrard, J. W., Sammons, H. G., Smellie, J. M. (1952) *Lancet*, **i**, 836.
Bennett, T. I., Hunter, D., Vaughan, J. M. (1932) *Quart. J. Med.* **1**, 603.
Cooke, W. T., Elkes, J. J., Frazer, A. C., Parkes, J., Peeney, A. P. L., Sammons, H. G., Thomas, G. (1946) *Ibid*, **15**, 141.
— Peeney, A. L. P., Hawkins, C. F. (1953) *Ibid*, **22**, 59.
Dicke, W. K. (1950) *Int. Congr. Pædiat.* p. 117.
— Weijers, H. A., van de Kamer, J. H. (1953) *Acta pædiat., Stockh.* **42**, 34.
Ebbs, J. H., Thompson, M., Stein, W. O. (1950) *Amer. J. Dis. Child.* **79**, 936.
Emery, J. L. (1947) *Arch. Dis. Childh.* **22**, 41.
Fanconi, G. (1928) *Schweiz. med. Wschr.* **58**, 789.
Farber, S., Shwachman, H., Maddock, C. L. (1943) *J. clin. Invest.* **22**, 827.
Fisher, O. D., Neill, D. W. (1955) *Lancet*, **i**, 334.
Frazer, A. C. (1952) *Trans. R. Soc. trop. Med. Hyg.* **46**, 576.
— (1953) *Acta gastro-ent. belg.* **16**, 491.
— French, J. M., Thompson, M. D. (1949) *Brit. J. Radiol.* **22**, 123.
French, J. M. (1955) *Proc. Nutr. Soc.* **14**, 33.
Gee, S. (1888) *St. Bart's Hosp. Rep.* **24**, 17.
Gerrard, J. W., Ross, C. A., Astley, R., French, J. M., Smellie, J. M. (1955a) *Quart. J. Med.* **24**, 23.
— — Smellie, J. M. (1955b) *Lancet*, **i**, 587.
Grette, K., Imerslund, O. (1953) *Tidsskr. norske Laegeforen.* **73**, 695.
Haas, S. V. (1924) *Amer. J. Dis. Child.* **28**, 421.
Hardwick, C. (1939) *Arch. Dis. Childh.* **14**, 279.
Howland, J. (1921) *Trans. Amer. Pediat. Soc.* **33**, 11.
Kralnick, H. G., Debatin, F. (1954) *Mschr. Kinderheilk.* **102**, 407.
Lowe, C. V., May, C. D. (1951) *Amer. J. Dis. Child.* **82**, 459.
Macrae, D., Morris, N. (1931) *Arch. Dis. Childh.* **6**, 75.
May, C. D., McCreary, J. F. (1940) *J. Pediat.* **17**, 143.
— — Blackfan, K. D. (1942) *Ibid*, **21**, 289.
Miller, R., Webster, J., Perkins, H. (1920) *Lancet*, **ii**, 894.
Morris, N., Peden, O. D. (1937) *Quart. J. Med.* **6**, 211.


*References continued at foot of next column*

# SERUM-CHOLESTEROL, DIET, AND CORONARY HEART-DISEASE

## AN INTER-RACIAL SURVEY IN THE CAPE PENINSULA


B. BRONTE-STEWART
M.D. Cape Town, M.R.C.P.
PHYSICIAN

A. KEYS
Ph.D. California, Ph.D. Camb.
PROFESSOR AND DIRECTOR, LABORATORY OF PHYSIOLOGICAL HYGIENE, UNIVERSITY OF MINNESOTA

J. F. BROCK
D.M. Oxfd, F.R.C.P.
PROFESSOR OF MEDICINE IN THE UNIVERSITY OF CAPE TOWN

*With the collaboration of*

A. D. MOODIE, A.M.I.A. — M. H. KEYS, A.B. — A. ANTONIS, Ph.D., A.R.I.C.

*From the Clinical Nutrition Unit, Department of Medicine, University of Cape Town, South Africa, and the Laboratory of Physiological Hygiene, School of Public Health, University of Minnesota, Minneapolis, U.S.A.*


THROUGHOUT the Western World there is anxiety over the high and apparently increasing death-rate from coronary heart-disease.* Those in the professional, executive, and more highly skilled occupational classes are particularly susceptible (Registrar-General 1954)—men our community can little afford to lose. Wide differences in susceptibility to the effects of coronary heart-disease exist between different countries or races, while within the same country a difference in prevalence has been noted during certain periods, such as the last world war (Malmros 1950, Strøm and Jensen 1951).

Apart from age and sex, many factors probably govern this susceptibility. Genetic influences, exposure to infections, and the geographic and climatic environments have been advanced as adequate explanations for the differing incidence from race to race. Keys, on the other hand, has demonstrated that, in those countries where the death-rate from coronary heart-disease is low, the population consumes less fat and exhibits a low mean serum-cholesterol level (Keys et al 1952, Keys 1954a and b, Keys, Fidanza, et al. 1954, Keys, Vivanco, et al. 1954, Keys and Anderson 1954). In fact a statistically significant relationship has been demonstrated between the death-rate from coronary heart-disease, the mean serum-cholesterol level, and the proportion of calories derived from total dietary fat.

In Cape Town we are in the favourable position of having a multiracial community living in the same climate, with each race in the main adhering to its traditional customs, particularly as regards diet. In part the dietary habits depend on purchasing-power; but even among the poorer Europeans the mean percentage of calories derived from fat is more than double

* Here we use this term in the sense of the effects of myocardial ischæmia arising from narrowing or occlusion of a coronary artery due to atherosclerosis and/or thrombosis.

### DR. SHELDON : REFERENCES—*continued*


Parsons, L. G. (1932) *Amer. J. Dis. Child.* **43**, 1293.
Paterson, D., Pierce, M., Peck, E. (1944) *Arch. Dis. Childh.* **19**, 99.
Ragazzini, R., Bartolozzi, G., Pratesi, E. (1953) *Div. di Clin. Ped. (Florence)* **52**, 223.
Ross, C., Frazer, A. C., French, J. M., Gerrard, J. W., Sammons, H. G., Smellie, J. M. (1955) *Lancet*, **i**, 1087.
Sheldon, W. (1949) *Arch. Dis. Childh.* **24**, 81.
— (1954) *Postgrad. med. J.* **15**, 79.
— Lawson, D. (1952) *Lancet*, **ii**, 902.
— MacMahon, A. (1949) *Arch. Dis. Childh.* **24**, 245.
— — (1951) *Ibid*, **26**, 446.
Still, G. F. (1918) *Lancet*, **ii**, 163, 193, 227.
van de Kamer, J. H., Huinluk, H. ten B., Weijers, H. A. (1949) *J. biol. Chem.* **177**, 347.
— Weijers, H. A., Dicke, W. K. (1953) *Acta pædiat.* **42**, 223.
Weijers, H. A., van de Kamer, J. H. (1950) *Int. Congr. Pædiat.* 118.

that of the Bantu (Batson 1953). The consumption of fat by the Cape Coloured lies midway between. The evidence, too, indicates that the morbidity and mortality from coronary heart-disease differ widely in these three racial groups.

We report here our findings in an inter-racial study in middle-aged men.

### Socio-economic Backgrounds

*Bantu*

In Cape Town the Bantu usually occupy the lowest socio-economic plane, providing mainly the unskilled labour. Those who earn least, usually heavy manual labourers, come to the city from the rural areas for short periods (six months to two years) hoping to save enough money to meet certain needs of their homes in the reserves. They want food that is both cheap and bulky, and nearly all of them rely much on maize-meal porridge and bread—often eating little else. This diet is low in both fat and protein and in addition it has a high residue (Walker and Arvidsson 1954). As the Bantu climbs the socio-economic scale, his diet still has the same basis of mealie meal and bread but tends to contain slightly more fat and protein: at his work he may buy *vet-koekies* (fat cakes—dough fried in oil) and fried fish. With a further increase in wages he may be able to afford meat, usually cooked as a stew, and dripping, mixed with his maize-meal porridge or applied to his bread.

There are, however, Bantu born and brought up in the city, whose education and diet approach those of the poorer European. Many of these are officials in Native Administration, chefs, cooks, shop-owners, and waiters. There are very few Bantu in the professional class as yet.

*Cape Coloured*

The Cape Coloured community originated mainly from European, Hottentot, and Malay admixture. Only within the last few decades could any Bantu blood have been added. A section known as the Cape Malays (of Moslem faith) are said to be relatively pure, being descendants of the artisans imported from Malaya by the Dutch East India Company in the 17th century, and their technical skill has been handed down from generation to generation. (In this survey most of the Malays had to be obtained from the tailoring trade and thus represent the more sedentary section.) For religious reasons the consumption of alcohol in the Malay group is said to be nil. Many non-Malay Cape Coloured people, however, consume a great deal of wine and spirits. In the socio-economic scale the Cape Coloured is intermediate between the Bantu and European, with overlapping on each side. They compete in both the unskilled and the skilled labour market, and, compared with the Bantu, a far greater proportion are professional men. As a population they are more stable because there are no migrants.

There is less monotony in their diet than in that of the Bantu. The Malay approaches the Indian in his liking for spices and curries, and boiled green vegetables are rarely eaten. Otherwise the diet of the Coloured is more like that of the European.

*European*

In general the Europeans are economically privileged. We had considerable difficulty in finding middle-aged European men earning less than £50 a month. Most of these were unskilled dock labourers whose work could hardly be called heavy manual labour. Such men usually live in subeconomic housing-estates where rents are low and the family do not need to attain the standard of living set by the European white-collar workers; so they probably have as much money available for food as have white-collar workers with twice their income.

Even at the lower economic levels, Cape Town Europeans consume more than twice as much fat—measured in the percentage contribution towards the total calories—as do the Bantu, while the Cape Coloureds come in between (Batson 1953). The diet and the general mode of life of the average Cape Town European is not unlike that of people of Western European descent residing elsewhere in the world.

### Cases Studied and Methods Used

The sample obtained during February–May, 1955, consisted of about 600 adult males actively engaged in their accustomed occupations in industries where large groups of men representing the three main racial groups were employed simultaneously. Each man was given a careful clinical examination, and certain anthropometric measurements were made, including skin folds to assess the amount of subcutaneous fat (Brozek 1953, Keys 1953). A 9-lead electrocardiogram was obtained, and the socio-economic status was assessed. Facts about the income, occupation, family size, consumption of tobacco and alcohol, degree of responsibility, and extent of physical activity at work were ascertained. In addition, the nature of each person's diet was assessed, particularly as regards consumption of fat-containing foods. The intake of fat was further subdivided into that from animal and that from vegetable sources. Figures denoting the degree of consumption of fat can be regarded as semi-quantitative only, because it was assumed that each person consumed an "average" helping. An oxalated sample and a plain sample of venous blood completed the examination.

This report deals with certain of the above aspects and is concerned exclusively with 383 men aged 40–58. Men with present or past evidence, clinical or electrocardiographical, of angina pectoris or of myocardial infarction were excluded; this involved 9 Europeans, 5 Cape Coloureds, and 1 Bantu (who had inconclusive electrocardiographic changes only). Another European was excluded because a xanthomatous nodule was found on his right elbow: and 1 European, 1 Cape Coloured, and 1 Bantu were excluded because of diabetes mellitus. No subject had to be excluded because the hæmatocrit and hæmoglobin level were outside the normal range. In no case did the iodine slide test (Mallen et al. 1950, Woolf 1951) reveal unsuspected liver disease. The total cholesterol in the serum was analysed in duplicate by the method currently used by Keys and others in Minnesota, Great Britain, Italy, Spain, Yugoslavia, and Sweden (Abell et al. 1952 modified by Anderson and Keys 1955). The cholesterol content of the α and β lipoprotein fractions separated on filter paper by electrophoresis was measured in a like manner. Duplicate samples were dispatched by air to the laboratory of Physiological Hygiene in Minneapolis. The total lipid in the serum was measured by the elution technique of Swahn (1953). The erythrocyte-sedimentation rate (E.S.R.) (Wintrobe 1946) was estimated to exclude unsuspected active disease.

### Findings

There was good agreement between the results of cholesterol determinations done in Cape Town and those done in Minneapolis on the duplicates ($r = 0.9859$ for 126 pairs of analyses). This agreement applied to both the total cholesterol and the cholesterol in the α and β

TABLE I—MEANS AND STANDARD DEVIATIONS FOR CLINICALLY HEALTHY MEN, AGED 40 TO 58, IN CAPE PENINSULA

| Item | Bantu | Coloured | European |
|---|---|---|---|
| No. of men | 132 | 118 | 114 |
| Age in years | 45·8 ±5·5 | 46·5 ±5·0 | 47·0 ±5·2 |
| Total cholesterol in serum (mg. per 100 ml.) | 166·3 ±47·2 | 204·1 ±54·8 | 234·0 ±52·9 |
| % of total cholesterol in β-lipoproteins (mg. per 100 ml.) | 71·9 ±10·1 | 76·8 ±9·9 | 82·6 ±7·1 |
| Total serum-lipids (mg. per 100 ml.) | 393·0 ±138·0 (N = 65) | 544·2 ±188·1 (N = 63) | 850·5 ±314·8 (N = 57) |

lipoprotein fractions. As the Cape Town determinations of total cholesterol were done on fresh sera, these levels are used here.

*Effect of Race*

After exclusions due to probable ill health, there remained 364 men aged 40–58. These were subdivided on the basis of race, and the mean total-cholesterol level in the serum is given for each race in table I. The differences in means between the races are highly significant ($P<0.001$).

There are highly significant differences too in the distribution of the cholesterol within the α and β lipoprotein fractions, the European having 82·6% (±7·15%) of the total cholesterol in the β fraction, and the Bantu 71·9% (±10·1%). The Cape Coloured again lies in between—76·8% (±9·9%). The mean absolute cholesterol level in the α-lipoprotein fraction (about 40 mg. per 100 ml.) shows no racial difference. As shown in fig. 1, these distinct inter-racial differences in the total cholesterol levels are due to differences in the absolute cholesterol content of the β-lipoprotein fraction.

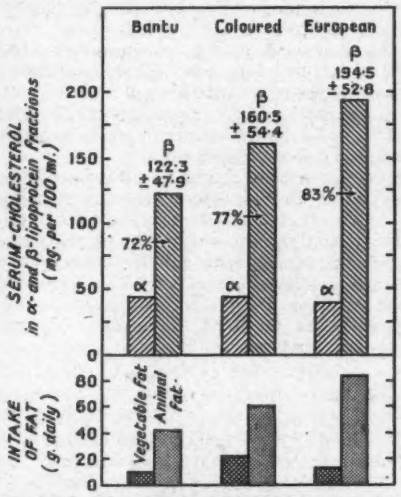



**Fig. 1—Mean consumption of fat and mean serum-cholesterol levels (in α and β lipoprotein fractions) in 363 men in Cape Town: 132 Bantu, 117 Coloured, and 114 European. Means and standard deviations for β-lipoprotein cholesterol were as follows: Bantu 122·3 ±47·9; Coloured 160·5 ±54·4; and European 194·5 ±52·8.**

*Effect of Raised E.S.R.*

One-third of the Bantu sample had an E.S.R. of 10 mm. or more in one hour, whereas only 12½% of the Cape Coloureds and 3½% of the Europeans had similarly raised E.S.R. No cause for this was obvious in the people concerned. Analysis with due allowance for race revealed a slightly lower mean serum-cholesterol level in those Bantu and Cape Coloureds with E.S.R. of 10 mm. or more in one hour (table II). These differences were not significant ($0.5>P>0.4$ for the Bantu and $0.9>P>0.8$ for the Cape Coloured sample). Consequently these people were not excluded from the survey.

*Effect of Socio-economic Status*

Despite the considerable inter-racial differences in mean serum-cholesterol levels there was considerable overlap from race to race. Income was then selected as a basis for further subdivision within each race. As regards the Bantu, a stepwise increase in the mean total-cholesterol level in the serum, and the cholesterol in the β-lipoprotein fraction in particular, paralleled the ascent from low to high income. The same trend appeared in the Cape Coloured, and to some extent in the European, though in the latter group the mean serum-cholesterol levels were almost identical in the low-income and middle-income groups. Otherwise, at the same income level, irrespective of race, almost identical total-cholesterol and β-cholesterol levels were found (fig. 2).

Income being used as a basis again, it was found that an increase in income was associated with an increase in consumption of fat—particularly fat of animal origin. The striking parallelism between the increase in cholesterol levels and the increase in consumption of animal fat with a rise in income is shown in fig. 2. Again, as in the case of the serum-cholesterol, the mean consumption of animal fat of subgroups at the same economic plane was much the same irrespective of race. Furthermore it was evident that Europeans with low and middle incomes, who could not have been separated on the basis of cholesterol levels, consumed similar amounts of animal fat. To date the small group of 17 Cape Malays studied have a higher mean serum-cholesterol than Cape Coloureds of the same economic class, and their consumption of animal fat is also higher. The differences, however, are not significant. In no group did any parallelism emerge between the estimated intake of vegetable fat and the mean total-cholesterol or β-lipoprotein-cholesterol levels in the serum (figs. 1 and 2). But it will be noted that the vegetable-fat values are very low, and no great reliance can be put on them, as the small amounts present in fruits, nuts, and cereals were not taken into account.

TABLE II—MEANS AND STANDARD DEVIATIONS FOR SERUM-CHOLESTEROL AMONG BANTU AND COLOURED MEN CLASSIFIED ACCORDING TO E.S.R.

| | No. of persons | Serum-cholesterol level (mg. per 100 ml.) | |
|---|---|---|---|
| | | Total | β-lipoprotein |
| *Bantu:* | | | |
| E.S.R. <10 mm. in 1 hr. .. | 88 | 168·3 ±46·5 | 71·7 ±10·6 |
| E.S.R. 10 mm. or more in 1 hr. .. .. .. | 44 | 162·2 ±48·9 | 72·1 ±9·0 |
| *Coloured:* | | | |
| E.S.R. <10 mm. in 1 hr. .. | 103 | 204·6 ±53·9 | 76·8 ±9·8 |
| E.S.R. 10 mm. or more in 1 hr. .. .. .. | 15 | 200·3 ±64·6 | 77·0 ±10·6* (only 14 persons) |

## Discussion

In Cape Town the death-rate ascribed to coronary heart-disease, in persons aged 35 or over, is more than twice as high in those of pure European descent as it is in Cape Coloureds (Cape Town 1946). In the Bantu townships of this city registration of a death as due to coronary heart-disease is exceedingly rare: possibly 1 to 3 are so registered each year (Cape Town 1952). The comparative rarity of coronary heart-disease is reflected

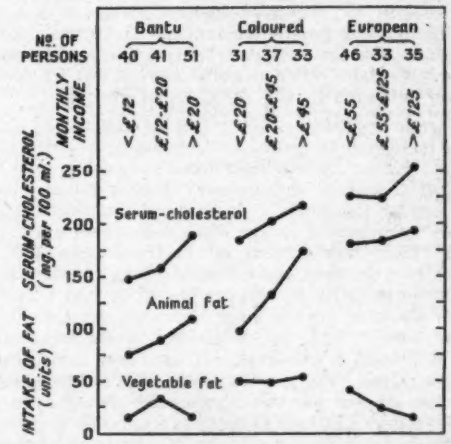



**Fig. 2—Mean total-cholesterol levels in serum, and mean weekly intakes of fat (1 unit of fat = 3·15 g.), of three special groups classed according to monthly income: Bantu, less than £12, £12–20, and over £20; Coloured, less than £20, £20–45, and over £45; and European, less than £55, £55–125, and over £125.**

in our hospital statistics, clinical observations, and post-mortem studies, and in attendances at our cardiac clinic (Vogelpoel and Schrire 1955). Similar views are held about Bantu elsewhere in South Africa (Becker 1946, Elliott 1953, Higginson and Pepler 1954) and in Uganda (Davies 1948). The small experience of this survey confirms these views. In our series only 1 Bantu had to be excluded because of probable past experience of heart-disease due to coronary atherosclerosis, whereas in the European sample the number was 9 and in the Cape Coloured it was 5.

The relationship between a high serum-cholesterol level and predisposition to coronary heart-disease is now well established. The remarkable parallelism between the Cape Town racial experience of coronary heart-disease and the mean levels of serum-cholesterol in table I is consequently worthy of note. It is possible therefore that in the reasons for the inter-racial differences in mean serum-cholesterol level may be found the reasons for the differing racial susceptibility to coronary heart-disease.

## GENETIC OR RACIAL FACTORS

Brink (1949) reported that the Bantu possess an extra coronary artery. Elliott (1953) has discussed the evidence against this being a factor of any importance, and Singer (1955) has found the same coronary-branch anomalies in European hearts. Despite the significant difference in mean serum-cholesterol levels between the Bantu and Cape Coloured samples, subdivision of the racial groups on the basis of income revealed approximately identical levels for Bantu and Cape Coloured subjects at the same economic level. It is unlikely that genetic factors account for this, because no appreciable Bantu admixture with the Cape Coloured community has occurred until the last few decades, if then. At the same economic level, however, the Cape Malay, said to be genetically distinct from the Cape Coloured, exhibits a higher mean serum-cholesterol level. In view of the presence of more obviously influential environmental factors, it is unnecessary at this time to speculate about conceivable genetic factors (Glass 1955). These views are in agreement with comparisons on population subgroups in other countries, such as Spain (Keys, Vivanco, et al. 1954), Italy (Keys, Fidanza, et al. 1954), and in South Africa (Walker and Arvidsson 1954).

## ENVIRONMENTAL INFLUENCES

In the present study geographic and climatic environments cannot be invoked to explain the inter-racial differences in the serum-cholesterol levels, as has been suggested in other population surveys. Likewise variables of age and sex are excluded by the composition of the sample. Certain other definite environmental factors, however, distinguish the three racial groups.

*Exposure to Infection*

The incidence of parasitic and bacterial infection is certainly higher among both non-European groups than among Europeans, and possibly higher among Bantu than among Coloureds. A raised E.S.R. (estimated to disclose unsuspected active disease in these apparently healthy men) was commonest in the Bantu (33½%), less common in the Cape Coloured (12½%), and rare in the European (3½%). Mass radiography had been done at their places of work in most instances, and the subjects of this survey had not originated from areas where tropical disease is endemic. If infection is responsible for these raised sedimentation-rates, it is unlikely to play a part in the low serum-cholesterol levels; for we were unable to show that the differences were significant. The correlation both here and in other parts of the world between the incidence of parasitic and bacterial infections and the experience of heart-disease due to coronary atherosclerosis would suggest that if infections or infestations play any part at all they protect against severe coronary atherosclerosis—a conclusion which is, however, neither justified nor otherwise acceptable.

*Personal Habits and Social Customs*

Generally the Cape Coloureds, having adopted in the main the Western European way of life, stand closer to the European than do the Bantu. The consumption of alcohol probably decreases through the groups in the following order: Cape Coloured, European, Bantu, Cape Malay (the last being abstainers). The smoking habits of the upper-income Cape Coloured groups do not differ recognisably from those of the European, but the Bantu smoke pipes much more than cigarettes.

*Physical and Mental Activity*

There is reason to believe that the degree of physical activity may influence the development or effects of coronary heart-disease and the level of the serum-cholesterol (Morris et al. 1953, Biörck et al. 1954). In Cape Town the Bantu form, in the main, the heavy manual-labour force, whereas the Europeans are more sedentary, even in their mode of travel. In considering the possible effects of physical activity allowance must be made for the increased caloric consumption that heightened physical activity demands. There are further difficulties in assessing the effects of physical activity and, for that matter, occupational trends (Registrar-General 1954) in that it is usual for sedentary workers to earn more money and carry more responsibility.

Mental stress has often been thought to have a rôle in coronary heart-disease, though there is no convincing evidence of this (Arnott 1954). In any case it is too difficult a factor to analyse comparatively in the three racial groups. If supervisory responsibility at work be taken as a measure of mental stress, then the European is more exposed in Cape Town. On the other hand, the non-European bears more of the stresses accompanying poverty and insecurity.

*Diet*

In general the dietary customs of the three racial groups are different, and there is a great deal of evidence for a major effect of diet on the serum-cholesterol level and on the development of coronary heart-disease. The customary Bantu diet is rich in carbohydrate but low in fat, protein, and many vitamins. It is held (Brock 1955) that chronic protein malnutrition accounts for the fact that throughout Southern Africa there is a fair incidence of testicular atrophy, gynæcomastia, and fibrosis of the liver in apparently well-nourished Bantu (Gillman and Gillman 1951). These features were not evident among the subjects in this survey. The iodine slide test, used as a screen for occult liver disease, gave no positive result, and Walker and Arvidsson (1954) could find no significant differences between the mean serum-cholesterol levels of their Bantu groups with and without positive tests for liver disease.

Excess of calories and its expression in relative obesity cannot be of more than secondary importance. Among Englishmen and Italians studied (Keys and Keys 1954) the Italians were more obese, but the Englishmen had a higher mean serum-cholesterol and a greater incidence of coronary heart-disease due to coronary atherosclerosis. Where this disease is very common, as in the U.S.A., the distribution of relative obesity among patients with coronary heart-disease differs little from the distribution among the healthy population (Keys 1954a, 1955). Our preliminary data on obesity and serum-cholesterol levels in the European and Coloured population in Cape Town are in general agreement with the above views.

Of all the dietary items for consideration, it is the proportion of fat in the diet that bears the closest relationship to the frequency of coronary heart-disease and the height of the blood-cholesterol. This relationship is highly consistent over the whole range of diets of populations studied, from 8% of calories derived from

fat in Japan (Keys and Anderson 1954) to more than 40% in the U.S.A. The fall in mortality from coronary heart-disease in Norway during the war coincided with a fall in consumption of fat (Strøm and Jensen 1951, Pihl 1952). Very low serum-cholesterol levels were observed during the war among persons on scanty low-fat rations (Brull et al. 1945, Simonart 1948, Gsell 1948), and a significant rise in mean serum-cholesterol levels in Germany from 1947 to 1949 was attributed by Schettler (1950) to increase intake of fat.

From Batson's (1953) survey of the diets of the main population groups in the Cape Town area it appears that, on the average, the Bantu gets about 17% of his calories from fats, a figure to be compared with about 25% for the Coloureds and 35% for the Europeans of low economic status. Our own survey does not enable us to express the intake of fat exactly in this way, but our samples of men evidently conformed roughly to this pattern. The Europeans with a high income undoubtedly derive a larger proportion of calories from fats than do the other Europeans, but whether the figure equals the 40+% currently recorded in the U.S.A. (see Keys 1954b) cannot be said. The average serum-cholesterol level for the combined European men is slightly lower than the average for men of the same age in Minnesota, and this corresponds well to what is known of the diets involved.

In different populations there is a striking correlation between the mean serum-cholesterol level and the percentage of calories derived from fat. The same striking correlation is noted in our three groups. On subdivision of each of our racial groups on the basis of income two trends emerged. As the income increased within each racial group, the mean serum-cholesterol rose and the mean consumption of animal fat increased. At the same income level, irrespective of race, the mean serum-cholesterol levels were almost identical, as were the means of consumption of animal fat.

In no instance did the mean consumption of vegetable fat correlate well with the mean serum-cholesterol levels of the subgroups. This adds weight to the studies of Groen et al. (1952) and Kinsell (1954) on vegetable-fat feeding and the studies by Donath et al. (1953) and Hardinge and Stare (1954) on true vegetarians. Possibly more importance should be attached to the nature of vegetable products in the diet to account for the conflicting views held on this matter (Mayer et al. 1954, Ahrens et al. 1955). Furthermore, diets rich in animal fat are characterised by liberal quantities of animal-protein foodstuffs with resulting vitamin changes and by decreasing quantities of starch and cellulose. Further work is indicated along these lines.

The reason why the dietary fat tends to control the blood-cholesterol and lipoprotein levels and hence to dominate coronary heart-disease is apparently the simple fact that fats as such are insoluble in blood-plasma or other watery media in the body. Lipoproteins are readily soluble. To be absorbed and transported about the body, fats must be combined with cholesterol and proteins in the soluble form of lipoproteins (Russ et al. 1951, Oncley and Gurd 1953).

The close parallelism between the incidence of coronary heart-disease, the serum-cholesterol level, and the percentage of fat in the diet, supported by experimental and theoretical evidence for a true causal connection, offers the greatest hope for effective prevention and control of the morbidity and mortality from coronary heart-disease. Certainly few problems merit more intensive study at present.

## Summary

A study was made of the bodily characteristics, serum-cholesterol and serum-lipoprotein levels, diet, and personal habits of 383 men, aged 40 to 58, residing in the Cape Peninsula. These men were selected as being reasonably representative of three racial groups—Bantu, Cape Coloured, and European—which differ strikingly in the prevalence of coronary heart-disease. 9 Europeans, 5 Cape Coloureds, and 1 Bantu were excluded because of evidence for probable coronary heart-disease, and 4 men were excluded on other medical grounds.

Highly significant differences in the mean total-cholesterol level, and particularly in the cholesterol level in the β-lipoprotein fraction of the serum, were found when the men were classified according to their racial origin. The Bantu lay at one extreme and the Europeans at the other. The Cape Coloureds were between.

There are large differences between these racial groups as regards their average diets, particularly the habitual consumption of fat. The fat-consumption of the Europeans is more than twice that of the Bantu, with the Coloured group intermediate.

Further subdivision within these three racial groups on the basis of income revealed that with an increase in income from subgroup to subgroup two consistent and paralleled trends emerged:

(1) An increase of the mean total cholesterol in the serum, and particularly of the β-lipoprotein fraction.

(2) An increase in the consumption of food containing fat, particularly animal fat.

At any given income level, the mean level of total cholesterol, and of β-lipoprotein cholesterol, was much the same for the three races; and so was the mean level of consumption of animal fat.

The results of this survey support the hypothesis that the dietary intake of fat influences the level of the serum-cholesterol, particularly that in the β-lipoproteins, and in turn may be one of the major factors influencing the pathogenesis of coronary heart-disease.

This study was undertaken as part of the programme of the Research Unit in Clinical Nutrition supported in the University of Cape Town by the Council for Scientific and Industrial Research. Part of the cost was defrayed from the research funds supplied to Dr. Ancel Keys from the National Dairy Council, Chicago, and the American Heart Association, New York.

We wish to acknowledge the technical and other assistance given by Miss C. Niland, B.SC., Miss J. Ethelston, B.SC., Miss E. Black, B.SC., Miss S. Newman, Miss E. Sophangisa, Mrs. E. Pallett, Mr. G. F. J. Schoonraad, and Mr. T. J. Turner. Dr. R. Singer, assisted by Mr. A. Mdingi, was responsible for the anthropometry, and Dr. B. Kaplan, assisted by Mr. D. Deppa, for the electrocardiography. Dr. Joseph T. Anderson was responsible for the analysis of specimens sent to Minneapolis.

Finally we should like to record our appreciation of the magnificant response to our appeal for volunteers by the male community of Cape Town and to the various organisations and industries, including Rotary, the City Corporation, the South African Railways and Harbours, and others, which sacrificed man-hours for the sake of this survey.

## REFERENCES

Abell, L. L., Levy, B. B., Brodie, B. B., Kendall, F. E. (1952) *J. biol. Chem.* **195**, 357.
Ahrens, E. H. jun., Tsaltas, T. T., Hirsch, J., Insull, W. jun. (1955 *J. clin. Invest.* **34**, 918.
Anderson, J. T., Keys, A. (1955) *Clin. Chem.* (in the press).
Arnott, W. M. (1954) *Lancet*, **i**, 1251.
Batson, E. (1953) *J. social Res., Pretoria*, **4**, 113.
Becker, B. J. P. (1946) *S. Afr. J. med. Sci.* **11**, 97.
Björck, G., Overbeck, W., Grönvall, C. (1954) *Cardiologia*, **25**, 232.
Brink, A. J. (1949) *Clin. Proc.* **8**, 137.
Brock, J. F. (1955) *Nutr. Rev.* **13**, 1.
Brozek, J. (1953) *Amer. J. phys. Anthropol.* **11**, 147.
Brull, L., et al. (1945) Les états de carence en Belgique pendant l'occupation allemande 1940–1944. Liége; p. 47.
Cape Town (1946) Annual Report of Medical Officer of Health, p. 84; Seventh Population Census of Union of South Africa, 7th May, 1946; vol. 2, pp. 40, 148.
— (1952) Annual Report of Medical Officer of Health; pp. 102, 108.
Davies, J. N. P. (1948) *East Afr. med. J.* **25**, 454.
Donath, W. F., Fischer, I. A., van der Meulen-van Eysbergen, H. C., de Wijn, J. F. (1953) *Voeding*, **14**, 153.
Elliott, G. A. (1953) *The Leech*, **23**, 25.

*References continued overleaf*

# MYOCARDIAL INFARCTION
## ITS RACIAL INCIDENCE IN CAPE TOWN

L. VOGELPOEL
M.B. Cape Town, M.R.C.P.
PHYSICIAN

V. SCHRIRE
M.B., Ph.D., M.Sc. Cape Town, M.R.C.P., M.R.C.P.E.
PHYSICIAN

*From the Cardiac Clinic, Groote Schuur Hospital, and the University of Cape Town, South Africa*

IN Cape Town there has long been an impression that coronary heart-disease is very uncommon in the Bantu and more common in the European than in the Cape Coloured population (Bronte-Stewart et al. 1955). We have tested the validity of this impression by a preliminary analysis of the electrocardiograms of adult inpatients and outpatients attending Groote Schuur Hospital. With its 842 beds and 300,000 outpatient attendances yearly, this is the main hospital serving the 500,000 population of Cape Town, which is divided among Europeans, Cape Coloureds, and Bantu in the ratio of 2 : 2 : 1.

The clientele of the hospital is selected, because a means test prevents the attendance of all but the poorer section of the community. Almost all the non-Europeans are eligible, but only the poorer Europeans. Hence the hospital incidence of coronary heart-disease reflects the true incidence of this disease more accurately for the non-European than for the European population. In 1953 and 1954 attendances of adults at the medical outpatient section totalled 84,704, of which 45,506 were of non-Europeans. Of the 38,235 adults admitted to the wards 19,458 were non-Europeans.

### Findings

During 1953 and 1954 the number of electrocardiograms requested for adults was 5004. Twice as many were requested for Europeans as for non-Europeans (table I), though more of the latter attended the hospital. This suggests that attention is more often directed to the heart in the European.

Of the 5004 electrocardiograms 550 showed the classical pattern of myocardial infarction—448 (81·5%) in Europeans, 100 (18·1%) in Coloured, and only 2 (0·4%) in Bantu (table I).

Rigid criteria were used in the diagnosis of myocardial infarction. Abnormal T wave and S-T segment changes alone were never accepted. In anterior infarction wide or deep Q waves in the precordial leads (V1 to V7) or diminution in the R waves across the precordium were required in addition to T-wave inversion or S-T segment change. In posterior infarction a Q wave of at least 0·04 sec. in width or a Q wave deeper than 30% of the R wave in AVF was accepted. In the presence of right bundle-branch block a Q wave of 0·04 sec. in AVF or abnormally wide Q waves in the precordial leads indicated infarction. Infarction was very seldom diagnosed in the presence of left bundle-branch block; the presence of a Q wave and gross S-T segment depression over the left ventricle were then demanded.

TABLE I—RACIAL INCIDENCE OF MYOCARDIAL INFARCTION DETERMINED ELECTROCARDIOGRAPHICALLY IN ADULTS ATTENDING GROOTE SCHUUR HOSPITAL

| Race | Racial distribution of electrocardiograms | | Racial distribution of infarct patterns | | Percentage of races in 550 infarcts | Percentage of electrocardiograms showing infarcts |
|---|---|---|---|---|---|---|
| | No. | Ratio | No. | Ratio | | |
| European | 3309 | 1·95 | 448 | 4·4 | 81·5 | 13·54 |
| Coloured .. | 1471 | 1 | 100 | 1 | 18·1 | 6·80 |
| Bantu .. | 224 | | 2 | | 0·4 | 0·9 |
| Total .. | 5004 | .. | 550 | .. | .. | .. |

Although more Europeans were electrocardiographed than non-Europeans, the ratio was only about 2 : 1 and cannot be offered as the sole explanation for the striking difference found in the racial incidence of myocardial infarction. That there is an actual difference is shown by expressing the number of infarctions as a percentage of the total number of electrocardiograms taken for each racial group. Thus 100 electrocardiograms of Europeans included 13·54 infarctions; 100 electrocardiograms of Coloured included 6·80 infarctions; and 100 electrocardiograms of Bantus included 0·9 infarctions. Furthermore it is unlikely that age alone accounts for this differing incidence, because $\chi^2$ analysis reveals no statistical difference in the age-distribution of myocardial infarction by decade between 30 and 59 in the two groups (table II).

### Conclusion

5004 electrocardiograms of adults attending Groote Schuur Hospital were analysed to determine racial incidence of myocardial infarction.

TABLE II—DISTRIBUTION OF MYOCARDIAL INFARCTION BY DECADE FROM 30 TO 59 IN EUROPEANS AND NON-EUROPEANS ($0·2 > P > 0·1$)

| Age (yr.) | Europeans | Non-Europeans |
|---|---|---|
| | No. | No. |
| 30–39 .. | 16 (6·75%) | 7 (9·72%) |
| 40–49 .. | 85 (35·86%) | 33 (45·83%) |
| 50–59 .. | 136 (57·38%) | 32 (44·44%) |
| Total .. | 237 | 72 |

DR. BRONTE-STEWART AND OTHERS: REFERENCES—*contd.*

Gillman, J., Gillman, T. (1951) Perspectives in Human Malnutrition. New York; p. 429.
Glass, B. (1955) *J. chronic Dis.* **2**, 96.
Groen, J., Tjiong, B. K., Kamminga, C. E., Willebrands, A. F. (1952) *Voeding*, **13**, 556.
Gsell, O. (1948) *In* Hottinger, A., Gsell, O., Uehlinger, E., Salzmann, C., Labhart, A., Hungerkrankheit, Hungerödem, Hungertuberkulose. Basel; p. 161.
Hardinge, M. G., Stare, F. J. (1954) *Amer. J. clin. Nutr.* **2**, 83.
Higginson, J., Pepler, W. J. (1954) *J. clin. Invest.* **33**, 1366.
Keys, A. (1953) *In* Overeating, Overweight, and Obesity: Nutrition Symposium Series no. 6, National Vitamin Foundation, New York. Edited by R. S. Goodhart; p. 13.
— (1954a) *Amer. J. publ. Hlth.*, **44**, 864.
— (1954b) *In* Proceedings of the 42nd Annual Meeting of the Medical Section of the American Life Convention, Chicago; p. 163.
— (1955) *J. chronic Dis.* **1**, 456.
— Anderson, J. T. (1954) *In* Symposium on Atherosclerosis, National Academy of Sciences—National Research Council, publ. 338, Washington; p. 181.
— Fidanza, F., Scardi, V., Bergami, G. (1952) *Lancet*, ii, 209.
— — — — Keys, M. H., Di Lorenzo, F. (1954) *Arch. intern. Med.* **93**, 328.
— Keys, M. H. (1954) *Brit. J. Nutr.* **8**, 138.
— Vivanco, F., Rodriguez Miñon, J. L., Keys, M. H., Castro Mendoza, H. (1954) *Metabolism*, **3**, 195.
Kinsell, L. W. (1954) *J. Amer. diet. Ass.* **30**, 685.
Mallen, M. S., Ugalde, E. L., Balcazar, M. R., Bolivar, J. I., Meyran, S. (1950) *Amer. J. clin. Path.* **20**, 39.
Malmros, H. (1950) *Acta med. scand.* suppl. 246, p. 137.
Mayer, G. A., Connell, W. F., DeWolfe, M. S., Beveridge, J. M. R. (1954) *Amer. J. clin. Nutr.* **2**, 316.
Morris, J. N., Heady, J. A., Raffle, P. A. B., Roberts, C. G., Parks, J. W. (1953) *Lancet*, ii, 1053, 1111.
Oncley, J. L., Gurd, F. R. N. (1953) *In* Tullis, J. L., Blood Cells and Plasma Proteins. New York; p. 337.
Pihl, A. (1952) *Scand. J. clin. Lab. Invest.* **4**, 122.
Registrar-General (1954) Decennial Supplement England and Wales 1951 Occupational Mortality. London; part 1, p. 13.
Russ, E. M., Eder, H. A., Barr, D. P. (1951) *Amer. J. Med.* **11**, 468.
Schettler, G. (1950) *Klin. Wschr.* **28**, 565.
Simonart, E. (1948) La dénutrition de Guerre. Brussels and Paris.
Singer, R. (955) Personal communication.
Strøm, A., Jensen, R. A. (1951) *Lancet*, i, 126.
Swahn, B. (1953) *Scand. J. clin. Lab. Invest.* **5**, suppl. 9, p. 7.
Vogelpoel, L., Schrire, V. (1955) *Lancet*, ii, 1108.
Walker, A. R. P., Arvidsson, U. B. (1954) *J. clin. Invest.* **33**, 1358.
Wintrobe, M. M. (1946) Clinical Hematology. 2nd ed., Philadelphia; p. 226.
Woolf, C. R. (1951) *S. Afr. med. J.* **25**, 789.

Electrocardiographic evidence of myocardial infarction was very uncommon in the Bantu, being found in only 2 of 224 electrocardiograms.

Electrocardiographic evidence of myocardial infarction was found more commonly in the Cape Coloured than in the Bantu, and more commonly in the European than in the Cape Coloured.

The higher incidence of infarction in Europeans than in the non-Europeans was not due to a significant difference in age-distribution of the population studied.

We wish to thank Prof. J. F. Brock and Prof. Ancel Keys for their interest and encouragement. We are especially grateful to Dr. B. Bronte-Stewart for his criticism and help with the statistical analysis. One of us (L. V.) was in receipt of a grant from the Council for Scientific and Industrial Research through its Clinical Nutrition Research Unit.

REFERENCE

Bronte-Stewart, B., Keys, A., Brock, J. F. (1955) *Lancet*, ii, 1103.

## RIGHT THORACO-ABDOMINAL APPROACH FOR THORACIC ŒSOPHAGECTOMY

BRYAN P. MOORE
B.Sc., M.B. Lond., F.R.C.S.
SURGEON, THORACIC UNITS, SOUTH-EAST METROPOLITAN REGION

THE approach to thoracic œsophagectomy, mainly needed for carcinoma, has never yet been quite satisfactory, except for lesions of the cardia. In these cases a left oblique anterolateral thoracotomy in the bed of the eighth rib is extended through part of the abdominal wall towards the midline. This gives excellent access to the lower third of the œsophagus and to the stomach. It is, however, almost impossible to reach the upper third of the thoracic œsophagus by this way. If the anastomosis has to be done above the aortic arch, it is necessary to make a second intercostal incision in a higher rib-bed, usually the fourth, using the same skin incision.

In any operation for carcinoma of the œsophagus it is wise to obtain a generous clearance above the main growth because of the submucous lymphatic drainage, and therefore the anastomosis above the aortic arch is generally to be preferred. Mobilisation of the middle third of the œsophagus has to be done from the left of the aortic arch. The crucial point for operability of growths of the middle third is often the degree of infiltration and adherence around the tracheal bifurcation and the right main bronchus. The most important step in the operation is the removal of the growth, and for carcinoma of the middle third of the œsophagus this is done more satisfactorily from the right side than the left.

The usual right-sided approach to œsophagectomy, which is now commonly completed in one operation, consists of an upper abdominal incision and separate right lateral thoracotomy. If the stomach is mobilised before the thoracotomy, the growth may be found to be inoperable, and all this effort is misdirected. If the chest is opened first and the growth is found to be operable, the stomach must then be mobilised and a return made to the chest for the anastomosis. Usually this means that the patient will have to be turned twice instead of once. Turning the patient during a long and serious operation may cause a substantial deterioration in the cardiovascular condition.

A right thoraco-abdominal incision, similar to that used for the left side, gives an exposure which is hampered by the bulk of the liver and would probably make mobilisation of the stomach or of an intestinal loop difficult.

### Present Procedure

Although excellent results may be achieved by the above-mentioned methods, I have used what I believe to be a new approach in my last six thoracic œsophagectomies and three attempted œsophagectomies.

The patient is arranged supine on the operating-table with his right arm abducted to 90° and a small flat pillow or folded bath-towel placed transversely under the lower part of his thorax.

*The approach* is made in stages:

(1) After a usual skin preparation the line of the incision is infiltrated with ¼% lignocaine and 1/300,000 adrenaline. A left upper paramedian abdominal incision is made from midway between the umbilicus and costal margin up to the left side of the xiphoid cartilage. The abdomen is opened and a search made to exclude secondary deposits in the liver or in the glands around the cœliac axis. The operation can then be abandoned if necessary.

(2) The incision is extended in the midline up to the level of the fourth costal cartilage, and the sternum is split in the midline with a Lebsche chisel to the same level. The length of the bone which has to be divided is only about 5 cm.

(3) A right submammary incision is made from the midline to the mid-axilla over the fourth costal cartilage and rib. This incision is deepened through pectoral and serratus anterior muscles, and the lower borders of the fourth costal cartilage and rib are stripped. The rib-bed is incised and the pleural space opened. After the internal mammary vessels have been secured, the right half of the sternum at the level of the fourth interspace is cut transversely to join the midline section.

(4) A rib-spreader may now be inserted in the intercostal incision and fully opened, the separated angular sternal fragment being readily displaced downwards. The lung can be held forwards, downwards, or upwards by an assistant, giving thus a remarkably good access to the whole length of the thoracic œsophagus, which can be palpated, allowing its operability to be estimated. If there is doubt; the mobilisation can be started and, if found to be impossible, discontinued, and the wound closed. Alternatively a palliative operation can be planned.

In cases in which the growth is mobile a return may be made to the abdominal part of the wound:

The spreader placed in the midline between the sternal fragments affords an excellent approach to the upper part of the stomach and the œsophageal hiatus. The stomach is mobilised from the cardia to the region of the right gastric and right gastro-epiploic vessels. A small pyloroplasty can be done to counter the spasm otherwise produced by vagotomy. Next, the œsophageal hiatus in the diaphragm is widened by a small incision between sutures through the anterior fibres so that it will admit three finger-tips. The lower part of the œsophagus is mobilised through the hiatus. The stomach can now be drawn down a little and the cardia divided on the stomach side with the aid of de Martel's intestinal clamps. The proximal end of the stomach is now closed in a usual manner and the clamp removed. The intercostal incision is again spread and the œsophagus mobilised from below upwards, so that the growth and glands are stripped up to the apex of the chest. The cardia with its de Martel clamp can be easily and cleanly slipped through the hiatus into the right pleural space. The body of the stomach is next pulled up through the œsophageal hiatus into the right pleural space bimanually, and there is no difficulty in drawing the fundus up to the extreme apex of the pleural space.

*The anastomosis* can be done in the plane of the first rib, the end of the œsophagus being sutured to a small opening in the fundus of the stomach. A little traction on the mobilised œsophagus is a help, and an assistant can control the position of the fundus with a small sponge in a sponge-holder.

If extra clearance from a growth or a stricture is needed, the œsophagus can be freed a little way into the neck and drawn further down.

The technique of making the anastomosis depends on individual preference, the following method is suggested:

The end of the œsophagus can be sutured to the margin of an incision 2–3 cm. long in the fundus of the stomach. Continuous 20-day catgut may be used for the main suture line through all coats, and interrupted thread mattress sutures are convenient for support in the seromuscular layers. The œsophagus should not be cut completely away until the

inner layer of the anastomosis is nearly completed, because it can be used by the assistant to apply gentle traction. A few sutures to stitch the anterior mediastinal pleura to the stomach wall add to the security of the anastomosis. An additional assistance to the anastomosis is to pass a Ryle's tube down to the obstruction before the operation begins, and to thread it through the anastomosis, leaving it in situ after the end of the operation.

Should a Roux-en-Y loop be preferred to œsophagogastrostomy, the preparation and use would be equally accessible.

*Closure of the wound* presents no difficulty, but care should be exercised over the reapposition of the sternal fragment. Three simple stainless-steel wire sutures through the sternum may be used, and three catgut pericostal sutures assist the reapproximation of the ribs. The intercostal layer, the peritoneum, and the posterior rectal sheath may be repaired with continuous 'Mersilene.' The pectoralis muscle and fascia and the anterior rectus sheath have been repaired with fine continuous stainless-steel wire. The risk of contamination by infected material from the œsophagus or the stomach during this rather long and complicated operation cannot be ignored, and antibiotics should be placed in the pleural space and wound layers as a prophylactic measure. The pleural space should be drained through an axillary intercostal space for 36–48 hours to a bottle with a water-seal.

*Assistants*

Two assistants are necessary, one being placed to the operator's left but on the cephalic side of the patient's extended right arm, and the second standing on the patient's left.

An emphysematous lung reduces the pleural space and the room for manipulation. Excessive retraction of the lung may impede the filling of the right atrium and lead to a fall of the pulse pressure. The anæsthetist and the assistants must be aware of this danger.

*Anæsthesia.*—This approach does not create any special problem for the experienced thoracic anæsthetist.

## Case-reports

CASE 1.—A woman, aged 56, with a squamous carcinoma of the middle third of the œsophagus, 30 cm. from the incisor teeth.

*Operation* (Jan. 20, 1954).—Exploration revealed malignant infiltration of the posterior wall of the trachea, although this had not been detected on bronchoscopy, and the operation was abandoned. A Souttar's tube was placed in the stricture as a palliative measure. The patient left hospital in fair condition but died soon after of carcinomatosis.

CASE 2.—A man, aged 46, with a squamous carcinoma of the middle third of the œsophagus, 25 cm. from the incisor teeth.

*Operation* (Oct. 27, 1954).—Total thoracic œsophagectomy and end-to-side œsophagogastrostomy. Convalescence was complicated by a wound infection, but this healed after excision and secondary suture. The patient left hospital with good function, and no recurrence has been detected to date.

CASE 3.—A woman, aged 40, with a squamous carcinoma of the middle and lower thirds of the œsophagus 36 cm. from the incisors.

*Operation* (Nov. 17, 1954).—Exploration showed advanced metastases in glands round the cœliac axis, and the operation was abandoned. The patient left hospital in fair condition but died shortly after from carcinomatosis.

CASE 4.—A woman, aged 20, with multiple corrosive strictures of the œsophagus, starting 21 cm. from the incisors.

*Operation* (Dec. 1, 1954).—Total thoracic œsophagectomy with end-to-side œsophagogastrostomy. Convalescence was uncomplicated, and the patient left hospital with good function and has remained well.

CASE 5.—A boy, aged 16, with multiple corrosive strictures below 25 cm. from the incisors.

*Operation* (Feb. 9, 1955).—Total thoracic œsophagectomy and end-to-side œsophagogastrostomy. Convalescence was complicated by an empyema and a temporary leak from the anastomosis. After drainage of the empyema the anastomosis has soundly healed and the lung expanded. The patient has returned home with good function.

CASE 6.—A man, aged 42, with squamous carcinoma of the œsophagus at 31 cm. from the incisors.

*Operation* (Feb. 17, 1955).—Total thoracic œsophagectomy with end-to-side œsophagogastrostomy. Convalescence was uncomplicated, and the patient left hospital well and with good function. So far there has been no recurrence.

CASE 7.—A woman, aged 52, with squamous carcinoma of the œsophagus 33 cm. from the incisors.

*Operation* (March 16, 1955).—Exploration showed advanced metastases in glands round the cœliac axis, and the operation was abandoned. The patient returned home in fair condition and died shortly after from carcinomatosis.

CASE 8.—A man, aged 55, with squamous carcinoma of the œsophagus 30 cm. from the incisors.

*Operation* (Aug. 17, 1955).—Total thoracic œsophagectomy with end-to-side œsophagogastric anastomosis. The patient returned home a month after operation without complication.

CASE 9.—A man, aged 71, with squamous carcinoma of the œsophagus 30 cm. from the incisors.

*Operation* (Aug. 31, 1955).—Total thoracic œsophagectomy with end-to-side œsophagogastric anastomosis. The patient is well with good function, and the wound healed two weeks after operation.

## Discussion

Three of the patients were found to be inoperable, and no major palliative operation for their growths was thought to be advisable. They have since died.

Two had severe corrosive strictures. Both are now well, but one had a complicated convalescence with an empyema and temporary leak from the anastomosis, now both well healed.

Four have had resection for carcinoma and are alive and well ten months, six months, four weeks, and two weeks after operation. The first of these patients had a wound infection which required revision and secondary suture. This infection was attributed to contamination from the growth, which was particularly heavily infected.

A tenth patient, a boy aged 16, with a granulomatous stricture at and below 16 cm. from the incisors was also operated on. Thoracotomy showed that the lesion extended into the neck. For a first-stage procedure the thoracic œsophagus was excised and both its ends were closed. A gastrostomy was done at the same operation. On a following day a Roux-en-Y loop was mobilised, and so also was the cervical œsophagus through a left oblique incision in the neck. The loop was passed beneath the sternum up into the neck after the method of Robertson and Sargeant. In an effort to find healthy tissue for the anastomosis the œsophagus was trimmed back to the cricoid cartilage, but the wall was thick and unhealthy. An end-to-end anastomosis was done with difficulty.

It was not surprising that this leaked temporarily, but seven months after the operation the fistula and gastrostomy were soundly healed and the jejunal tube functioned well. In the light of these experiences, if the necessity for total œsophagectomy arises, I advise resection of the thoracic part and preparation of a Roux-en-Y loop by the right thoraco-abdominal approach described above, together with synchronous exposure and excision of the cervical œsophagus in the left side of the neck by an assistant. The anastomosis should be done with the loop of small bowel brought up behind the sternum.

It is well known that successful œsophagectomy requires tremendous attention to preoperative preparation and postoperative care. The operations are exacting and tedious, but I believe that this approach may prove to be an advantage to both patient and surgical team.

## Summary

An approach for thoracic œsophagectomy is described.

The approach is through left paramedian and fourth right intercostal incisions, which are joined through the

sternum. This wound can be widely spread in two directions.

The advantages include mobilisation of the œsophagus from the right side without need for turning the patient during the operation.

The length of the thoracic œsophagus which can be removed is unrestricted.

## RADIOPHOSPHORUS IN THE TREATMENT OF CAPILLARY NÆVI

D. S. ANDERSON ROE
M.D. Lond., M.R.C.P., D.C.H., D.M.R.T.
RESEARCH ASSOCIATE IN DERMATOLOGY, HOSPITAL OF THE UNIVERSITY OF PENNSYLVANIA; LATE CLINICAL ASSISTANT, RADIOTHERAPY DEPARTMENT, HOSPITAL FOR SICK CHILDREN, GREAT ORMOND STREET, LONDON

CHRISTINE HODGES
B.Sc., M.B. Wales, D.M.R.T.
CONSULTANT RADIOTHERAPIST, ST. JOHN'S HOSPITAL FOR DISEASES OF THE SKIN, LONDON

G. S. INNES
B.Sc. Aberd., A.M.I.E.E., A.Inst.P.
PRINCIPAL PHYSICIST, ST. BARTHOLOMEW'S HOSPITAL, LONDON; CONSULTANT PHYSICIST, HOSPITAL FOR SICK CHILDREN, GREAT ORMOND STREET

L. I. POPE
M.S.R., S.R.N.
SISTER, RADIOTHERAPY DEPARTMENT, HOSPITAL FOR SICK CHILDREN, GREAT ORMOND STREET

OF capillary nævi Brain and Calnan (1952) state: "The usual capillary nævi occur as small or large macules, with tints varying from the palest pink through shades of red to the deep purple of the port-wine stain mark, and the deeper the colour the worse the prognosis. Many of the pale pink birthmarks affecting the middle of the nape of the neck, and of the forehead tend to disappear spontaneously in a matter of weeks or months. Some of the red marks will fade, but the deeper red marks and purple marks persist." A similar observation on those marks affecting the nape of the neck was made by Bettley (1940).

Our investigation was confined to the deeper red and purple marks, which is what we mean here by capillary nævi.

The use of radium β-ray plaques for treating superficial lesions of the skin has diminished in England during the past decade for two reasons: the ease with which low-voltage X rays can be applied, and the fact that many of the existing radium β plaques are old and unreliable in their output of radiation. The Ministry of Supply, which some years ago took over the construction and supply of all radioactive appliances, felt that the use of radium for the construction of β plaques was not justified after the advent of emitters of pure β rays without gaseous daughter elements. However, it was some time before the Ministry solved the problem of separating the isotopes from the Harwell piles and of their loading into suitable containers. In any case the use of a rigid type of plaque of relatively small size restricts the usefulness of such plaques to the treatment of small areas on flat or only slightly curved surfaces.

When radioactive phosphorus became available in high concentrations at low cost, an improved type of β-ray plaque became feasible. Radioactive phosphorus ($^{32}P$) emits pure β rays with a maximal energy of 1·7 MeV and a mean effective energy of about 400 kV.

In 1946 the technique of making β-ray plaques with $^{32}P$ (Low-Beer 1946) was modified at St. Bartholomew's Hospital, London, as follows:

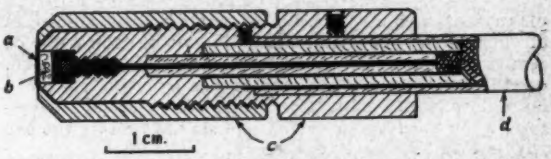



**Fig. 1—Section through ionisation chamber for measuring dosage from $^{32}P$ β-ray plaque: *a*, thin front wall equivalent to 23 μ of tissues; *b*, air volume 4 mm. in diameter and 1·5 mm. thick; *c*, perspex; *d*, cable to measuring instrument.**

A piece of blotting-paper of the same shape as, and slightly larger than, the lesion to be treated is ruled off into 0·5 cm. squares. A drop of $^{32}P$ solution is dropped on to the centre of each square from a syringe (ours delivers 0·008 ml. per drop). The blotting-paper is then dried in an oven at about 90°F. When dry the blotting-paper is loaded again, this time in the reverse direction to compensate for any unevenness in absorption or distribution during the first loading. If necessary, to get the required quantity of $^{32}P$ per sq. cm. the process can be repeated.

The dried blotting-paper is then mounted on lead which is 0·22 mm. thick and has a sticky adhesive surface. This lead acts as the protection medium for the back of the plaque. The front surface, which is to be the active treatment surface, is covered with one or two layers of 'Alkathene' sheet 0·004 in. thick.

A window-frame of lead, with an adhesive surface, of the size of the active area is made and placed over the front of the plaque, effectively sealing off the alkathene. As a final precaution against contamination of the staff or patient with $^{32}P$, the edges of the lead are sealed with 'Cellotape.' The sealing of these plaques has been so effective that they can be used with impunity even on moist surfaces without contaminating the patient.

Plaques constructed in the above-described manner give an output of 1000r an hour at the surface of a patient if loaded to a density of 265 μc of $^{32}P$ per sq. cm. of the plaque surface. The dosage-rate is measured with an ionisation chamber (fig. 1) which has a front wall of graphited cigarette paper which weighs 2·3 μg. per sq. cm. and only stops about 2% of the β rays. Radiation intensities of about 3000–4000r an hour are usually aimed at so that the treatment time is short and well tolerated by children.

$^{32}P$ has been loaded into flexible plastic at Harwell (Sinclair and Blondal 1952), but the output intensities are, in our opinion, too low—600–800r an hour.

The longest range of radiation of $^{32}P$ emitting β rays with a peak energy of 1·7 MeV is about 8 mm. in the tissues, but the average energy is such that, at a depth of 0·8 mm. in the tissues, the dosage-rate is only 50% of that at the surface (fig. 2). This restricts the application of these plaques, in our opinion, to lesions not thicker than 1 mm., unless one is prepared to give a necrotising dose to the surface layers.

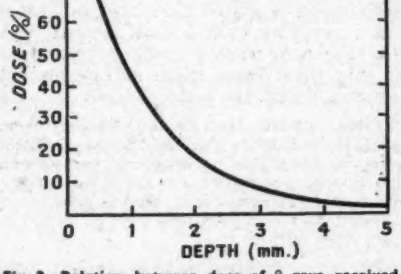



**Fig. 2—Relation between dose of β rays received by tissues from $^{32}P$ plaque and depth from surface of skin.**

The short range of the β particles makes the treatment of lesions lying over bone particularly safe, compared with treatment with radium

plaques or with X rays, and damage to the epiphyses of bones can be eliminated. It must, however, be remembered that, if an eyelid is being irradiated with one of our plaques, the underlying eye will receive a large dose, which may later produce a cataract. Therefore, when treating an eyelid, one should protect the eye with a lead 'Perspex' eye-shield.

### Method of Treatment

In a sheet of lead 0·2 mm. thick, with an adhesive surface, a central hole is cut so that the area of the lesion to be irradiated is defined by sticking the mask on to the patient's skin. The plaque is then placed over the lesion and strapped on. If the surface area is curved, the plaque is flexible enough to be shaped to fit snugly into any cavity or over any protuberance of the treated area. This shaping should be done with the operator wearing lead-rubber protective gloves. This flexibility of these plaques is one of their main advantages. Up to now plaques as large as 15 × 15 cm. have been constructed and used. It is safe to treat areas of this size on small children because, owing to the short range of the radiation in tissue, the effect on the hæmopoietic system is negligible. Local applications containing metallic oxides or salts, crusts, and exudates should be removed from the skin before the application of β-ray plaques, because foreign matter will absorb much of the radiation (Anderson et al. 1954).

Fig. 3—Capillary nævus: *a*, before treatment; *b*, 5 months after treatment with $^{32}P$.

### Discussion

The plaques were originally made for treating superficial malignant lesions, such as Bowen's disease and other intra-epidermal epitheliomas not thicker than 1 mm. The experience gained in treating these suggested that the plaques might be used to treat nævus flammeus, particularly those extensive ones which, on children's faces, can be so disfiguring, giving rise to psychological problems and causing much distress to the parents.

Very little informatiom seems to have been published on the dosage in r given to such lesions treated with radium β plaques. Exposure times for particular plaques were often cited, but these times mean nothing except in comparing treatments with the same plaque.

Investigation of the outputs of radium β plaques from different centres (British Empire Cancer Campaign 1953) showed that plaques of allegedly the same mg. per sq. cm. and same filtration gave outputs varying as much as 4 to 1, a ratio which, if the time of exposure used on the low-output plaque was transferred to the high-output plaque, would in many cases produce deep necrosis.

From observation of the treatments in malignant cases it was obvious that reactions were less per r for β rays than for X rays. One would expect this because the underlying tissues receive a larger dose from X rays than from β rays. Despite this experience we decided to start treating capillary nævi with doses which could not produce severe reactions and to increase the dose gradually until we attained the required effect.

On areas as large as 100 sq. cm. single doses of 450r and 700r produced no skin reaction but one of 900r did. Instead of increasing the dose we then followed the normal radiotherapy practice of delivering it in fractions over a few days. In a group of malignant cases treated at St. Bartholomew's Hospital this fractionation produced a better cosmetic result. We worked up from 2 × 450r to 2 × 700r to 3 × 450r, and we feel that it would be possible to go to 4 × 450r without producing severe reactions.

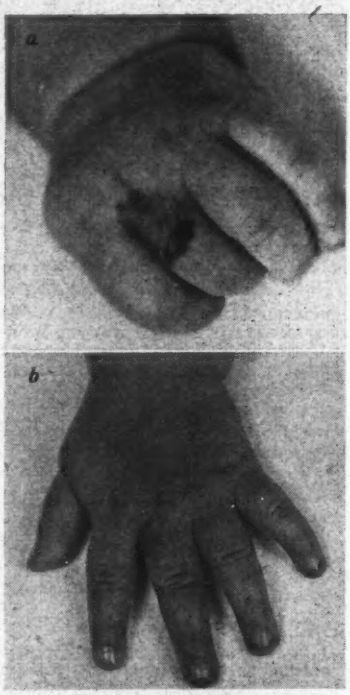



Fig. 4—Capillary nævus: *a*, before treatment; *b*, 9 months after treatment with $^{32}P$.

In many of the cases treated the areas had been previously subjected to extensive treatment with thorium-X with negligible improvement. The dose received from such treatment cannot be estimated since it depends on the method of painting on the thorium-X and how long it stays there. The dose may be exceedingly large and may be due to absorption in the tissues owing to cracks in the skin (British Empire Cancer Campaign 1953). In view of the uncertainty of this dose, the radiation given with the β plaques has often been less than we would have liked to give.

### Results

17 cases were treated with $^{32}P$ at Great Ormond Street Hospital for Sick Children between March 4 and Nov. 20, 1953. The early results appear to be encouraging, but a long follow-up of these cases for signs of skin atrophy is essential. The cosmetic result of larger doses of $^{32}P$ in the treatment of superficial skin carcinomata followed up over years has been excellent. In future the cavernous type, which practically always involutes spontaneously (Lister 1938, Brain and

Fig. 5—Capillary nævus: *a*, before treatment; *b*, 9 months after treatment with $^{32}P$.

Calnan 1952, Walter 1952) and is often too thick to be treated with β rays, will not be treated; but we feel that larger doses up to 1800–2250r fractionated over a week may be safely tried in capillary nævi, which are often tragically disfiguring and for which no other treatment offers such improvement without damaging the skin.

According to the children's mothers the resulting erythema began on or about the seventh day after treatment, except in 2 cases in which it is said to have started on the second and third days. 15 children showed signs of erythema when examined on the twenty-first day. In only 2 cases was scaling of the area reported. In all the cases the erythema had faded by the twenty-eighth day. So far 4 of the 17 nævi have virtually disappeared (as in figs. 3–5); 11 are definitely paler and still paling; and in 2 cases the results are not available.

### Summary

$^{32}P$ β-ray plaques have proved useful in the treatment of superficial vascular nævi, including capillary nævus, apart from the immense psychological effect on the parents that something is being done.

The plaques are easy to handle, can be shaped to fit into cavities and over protuberances, and can be made large or small as required.

They should not be used to treat lesions thicker than 1 mm.

If eyelids are being treated, the eyes must be protected.

Doses up to 3 × 450r have been given to nævus flammeus as large as 200 sq. cm. without any resultant severe skin reactions and have produced fading of the lesions.

Time alone will show whether there are any late skin changes with this dose, but after two years none have been observed.

We are indebted to Dr. R. T. Brain for permission to publish, and to Mr. Derek Martin, of the photographic department, Hospital for Sick Children, Great Ormond Street, for the photographs.

REFERENCES

Anderson, D. S., Williams, H. S., Stockley, A. V. (1954) *Brit. J. Derm.* **66**, 144.
Bettley, F. R. (1940) *Ibid*, **52**, 363.
Brain, R. T., Calnan, C. D. (1952) *Ibid*, **64**, 147.
British Empire Cancer Campaign (1953) Annual report; pp. 100, 101.
Lister, W. A. (1938) *Lancet*, **i**, 1429.
Low-Beer, B. V. A. (1946) *Radiology*, **47**, 213.
Sinclair, W. K., Blondal, H. (1952) *Brit. J. Radiol.* **25**, 360.
Walter, J. (1953) *J. Fac. Radiol., Lond.* **5**, 134.

## RUBELLA AS A CAUSE OF MENTAL DEFICIENCY

BRIAN H. KIRMAN
M.D. Lond., D.P.M.
DEPUTY PHYSICIAN-SUPERINTENDENT, FOUNTAIN HOSPITAL, LONDON

MENTAL retardation is due to genetic and environmental factors. In the case of low-grade defectives structural damage in the brain is usually demonstrable. In a minority of such idiots and imbeciles this damage is due to infection.

Among infections which are important in intra-uterine life the effect of syphilis has long been realised, but this disease is a very unusual cause of mental defect in this country today. The rôle of other infectious diseases is less certain. Burkinshaw et al. (1953) have shown that toxoplasmosis seldom causes mental defect. Gregg (1941) focused attention on rubella, and there is now no doubt that rubella in an expectant mother in the first four months of pregnancy can seriously damage the embryo. In some cases the effect is lethal and the result an abortion. If the infant survives, it may have mental defect, cataract, deafness, or heart defect. By analogy with damage due to rhesus incompatibility (Gerver and Day 1950) it seems likely that, even where the infant is considered to be normal, minor cerebral damage may reduce intelligence.

Estimates of the frequency with which infants exposed to risk are damaged vary. Few will agree with the view, put forward in the United States by Wesselhoeft (1949) and others, that the likelihood of damage is so great that abortion should be induced as a routine measure whenever an expectant mother has had rubella in early pregnancy.

Brown and Nathan (1954) found that 4 of 13 infants at risk had congenital deformities.

Grönvall and Selander (1948), in Sweden, found 28 cases of maternal rubella in more than 20,000 pregnancies: 2 ended in abortion, 25 healthy infants were born, and only 1 was malformed.

A study of an epidemic of rubella in Sweden (Lundström 1953) suggests that abortive attacks without clinical signs in an expectant mother can also cause embryopathy, the incidence of lesions in the embryo probably varying from one epidemic to another and with the mother's health and nutrition.

### Incidence of Rubella in Mentally Defective

The importance of rubella in mental deficiency is difficult to assess. The accompanying table shows details of 8 mentally defective children of mothers with a history of rubella. In 7 of them the mental deficiency is thought to be due to the maternal rubella. These 7 form about 0·9% of 791 mentally defective children in the Fountain Hospital group. Mongolism is responsible for 105 cases (13%) of mental deficiency in the same population. Rubella appears to be slightly more important than gargoylism as a cause of mental deficiency in the London area. The records of these children have been compiled over about six years, during which time no child with mental deficiency attributed to rubella has died, whereas many mongols have died. The proportion of mental defect due to rubella would therefore be still further reduced if the known cases were compared with a series of consecutive admissions.

Most of the children admitted to the Fountain Hospital are aged less than 5 years on admission, and most of them are either imbeciles or idiots. The number of cases discovered with a history of maternal rubella therefore indicates only the incidence of the severer degrees of brain damage and does not cover the minor degrees in children classed as educationally subnormal or higher. It is also probable that there are, in the population of this hospital, other mentally defective children whose defect is due to rubella but has not been diagnosed as such; some mothers may have had abortive attacks of rubella, and in others the rubella may not have been recognised.

The patients may remain in the hospital until the age of about 16, and in the case of many of the older children no specific question about rubella during pregnancy has been asked. Adequate histories, however, including this specific question, are available for almost all of the 790 new cases admitted during the past six years (this figure includes 50% of the present inpatient population of the hospital group).

In all 7 of the present cases the children were born in the three years 1943–45. The reason for this is not clear. A more careful search in those years is not the reason; in fact history-taking was more searching subsequently. There may have been a greater incidence of rubella, a heightened virulence of the infection, or possibly an alteration in the dietetic habits of expectant mothers towards the end of the war.

### Clinical Picture

The table shows that there is no very constant clinical picture beyond the association of mental defect with cataract in 4 of the 7 cases.

—ANALYSES OF CASES

| Case no. | Date of birth | Stage of pregnancy when rubella developed | Present age (yr.) | I.Q. | Ears | Eyes | Motor system | Other remarks |
|---|---|---|---|---|---|---|---|---|
| 1 | Nov. 24, 1944 | 3rd month | 10 | 16 | Deaf | Normal | Normal | Anæmic, rather schizoid |
| 2 | Oct. 28, 1944 | 1st month | 10 | 10 | ? Deaf | Blind, cataract, microphthalmia | Crawls, cannot walk | Very thin and weak |
| 3 | April 3, 1943 | 5th month | 11 | 16 | ? Normal | Normal | Normal | Rather schizoid |
| 4 | Jan. 10, 1943 | 1st month | 11 | 12 | ? Deaf | Blind, cataract, microphthalmia, nystagmus | Cerebral palsy, spastic | Congenital abnormality of heart (? pulmonary stenosis) |
| 5 | Jan. 24, 1945 | 2nd month | 9 | 56 | Normal | Blind, cataract, nystagmus | Normal | Mother thought it was ordinary measles she had and did not seek medical advice |
| 6 | April 20, 1945 | 2nd week | 9 | 4 | ? Deaf | Blind, cataract, microphthalmia, nystagmus | Cerebral palsy, hypotonia, tendon-jerks absent | Very underdeveloped physically |
| 7 | Oct. 20, 1950 | Doubtful | 4 | 12 | ? Deaf | Blind, cataract, microphthalmia | Cannot sit or stand | Another child is affected; this is probably not due to rubella |
| 8 | Sept. 16, 1945 | 2nd month | 9 | 17 | Normal | Normal except for strabismus | Normal | Some facial and digital deformity |

The relationship with deafness has been established by many workers—e.g., Ivstam (1951). In the present series only 1 child is definitely considered to be deaf. The uncertainty about the 4 shown as doubtfully deaf is due to the fact that at a low mental level, with limited responses to stimuli of any description, deafness is very difficult to establish with certainty.

The motor lesions are not characteristic: 2 children have cerebral palsy (i.e., they are more handicapped in their motor accomplishments than other idiots of the same level, and they have neurological signs); 1 child showed the usual features of spastic diplegia; and 1 was grossly hypotonic. In all 7 cases there was a degree of the infantilism which goes so commonly with severe mental defect.

The mental state was not easy to assess in view of the eye, ear, and motor lesions. In the 4 children shown as blind there was no useful vision despite operations, and in 3 the eyeballs were much shrunken. In spite of the difficulties, however, it can safely be assumed that 6 of the patients were idiots, since at no time, over years of observation, have they shown any evidence of higher intelligence. The other patient, a boy, is just within the educationally subnormal range but, in view of his double handicap, has remained in the occupation centre for the blind. Apart from intellectual limitation there are no special psychological features common to this group. None of these patients has had epilepsy. The 6 idiots require every attention, like small babies. The other boy (case 5) is clean in his habits, talks, walks well, is cooperative and friendly, feeds himself, helps in dressing, and plays games with the other children.

Case 7 was excluded from the series because the history of rubella is doubtful in her case, and a sibling has a cataract and a cerebral abnormality; this is probably an instance of familial cataract and is not due to rubella.

### Comments

Since the end of the last century there has been a tendency to emphasise the importance of genetic factors in mental deficiency. This trend is still apparent in modern textbooks. Wyllie (1953) cites Tredgold's (1929) view that 80% of mental defect can be classed as "primary."

Penrose's (1954) more critical approach has shown that much of the evidence of hereditary factors previously accepted is of little value, and that in perhaps only a third of all cases do genetic influences seem to be most important.

As time goes by, additional environmental factors in the causation of mental defect come to light. No single one of these, so far as we know, is responsible for any big group, but there seem to be a great many separate environmental factors each of which makes a small contribution to the sum total of cases of impaired mental function. Maternal rubella early in pregnancy is established as one such environmental factor; Lundström (1952) found the highest incidence of abnormalities at the second month but thought the true incidence in the first month might be higher still. Rubella is not a major factor but probably produces every year a small minority of the total of mental defectives.

With the increasing realisation of the importance of the environment in producing mental defect the prospects of prevention of at least some cases have become brighter. This also applies to rubella. Attempts at both active and passive immunisation of the mother have been made. Though the prophylactic value of γ-globulin is still open to question (Anderson and McLorinan 1953), some batches at least appear to have been effective (Bass et al. 1949, Korns 1952). J. C. McDonald (personal communication) states that the results of the use of γ-globulin in Britain to protect women exposed to rubella early in pregnancy are encouraging.

In view of the frequent occurrence of cataract in the present syndrome it is interesting to compare the cases attributed to rubella with the general incidence of cataract among mentally defective children. This association is common, and it seems that noxious factors which can damage the rapidly developing brain are also liable to injure the lens in early life. Apart from the minute cataracts which are such a common feature in mongolism (Lowe 1949) 61 patients at the Fountain Hospital have been noted as having gross and obvious cataract in the past six years, but only 7% of these are due to rubella.

Unfortunately, only 1 (case 5) of these 7 children can be considered as trainable. This group is, however, a sample of the most severe consequences of maternal rubella and cannot be regarded as representative. The poor success of eye surgery in these patients should not be taken as a contra-indication, since it is impossible to assess accurately the child's general capacity at the early age when treatment of cataract is usually undertaken, and even a small amount of vision will greatly facilitate the task of training. In the same way it is essential to test as early as possible all suitable patients for hearing, though this may be difficult where vision is also impaired, since the peep-show technique is not then applicable.

**Summary**

A history of rubella in early pregnancy was obtained from the mothers of 8 patients at the Fountain Hospital.

Rubella was thought to be responsible for mental defect and other anomalies in 7 of these cases.

These patients were found among 791 mentally defective persons, mostly children. They make up 0·9%.

All 7 children were born in 1943–45; 6 are untrainable idiots; 1 is above imbecile level but is blind; 4 are blind through cataract; deafness was established with certainty in 1 case.

There is no distinctive clinical picture apart from the combination of mental deficiency and cataract, with possibly deafness.

Maternal rubella is one of the very many causes of mental deficiency and brain damage which are being discovered. It accounts for only a small proportion of all cases of mental defect.

I wish to thank Dr. L. T. Hilliard for advice and help, Mrs. M. Marrs for psychological examination of the children, and Mr. L. Mushin for the eye reports.

REFERENCES

Anderson, S. G., McLorinan, H. (1953) *Med. J. Aust.* i, 182.
Bass, M., Davidson, H. B., Foote, F., Landon, J. F., Muckenfuss, R. (1949) *N.Y. Med.* **5**, no. 23, p. 21.
Brown, C. M., Nathan, B. J. (1954) *Lancet*, i, 975.
Burkinshaw, J., Kirman, B. H., Sorsby, A. (1953) *Brit. med. J.* i, 702.
Gerver, J. M., Day, R. (1950) *J. Pediat.* **36**, 342.
Gregg, N. M. (1941) *Trans. ophthal. Soc. Aust.* **3**, 35.
Grönvall, H., Selander, P. (1948) *Nord. Med.* **37**, 409.
Ivstam, B. (1951) *Acta otolaryng., Stockh.* **39**, 380.
Korns, R. F. (1952) *J. infect. Dis.* **90**, 183.
Lowe, R. F. (1949) *Brit. J. Ophthal.* **33**, 131.
Lundström, R. (1952) *Acta pædiatr., Stockh.* **41**, 583.
— (1953) *Svenska Läkartidn.* **50**, 97.
Penrose, L. S. (1954) The Biology of Mental Defect. London; p. 43.
Tredgold, A. F. (1929) Mental Deficiency (Amentia). London; p. 19.
Wesselhoeft, C. (1949) *New Engl. J. Med.* **240**, 258.
Wyllie, W. G. (1953) Garrod, Batten and Thursfield's Diseases of Children. Edited by A. A. Moncrieff and P. R. Evans. London; p. 1182.

# FAMILIAL HEMIPLEGIC MIGRAINE

J. N. BLAU
M.B. Lond., M.R.C.P.
C. W. M. WHITTY
M.A., D.M. Oxfd, M.R.C.P.
*From the Military Hospital for Head Injuries, Wheatley, and the Department of Neurology, Radcliffe Infirmary, Oxford*

HEMIPLEGIC migraine is an unusual variant of migraine, often with a strong familial tendency, in which the common visual aura is either superseded by or passes into hemiplegia, usually with associated hemianæsthesia and, if right-sided, aphasia.

Clarke (1910) published a history of hemiplegic migraine in 6 members in 3 generations of a family; Dynes (1939) in a mother and her daughter; Symonds (1952) in a father and his son, and in 3 males in 3 generations of another family; and Whitty (1953) in 3 further families.

We report here another family, in which 9 members in 4 generations were affected.

Although the associated family history of other and more usual forms of migraine, and the occasional occurrence of these in the same individual who has the hemiplegic variety, support the diagnosis of migraine, nevertheless many features are unlike those of classical migraine. Thus the headache may at times precede the hemiplegia, and some residual sensory and motor loss may persist for days. Neurological signs may also spread to the non-hemiplegic side for a time, and the attacks may be accompanied by severe confusion and even coma. Despite these seemingly alarming developments the condition remains benign, and complete recovery from a given attack is the rule.

The family history may be of decisive diagnostic value, for the complaint tends to have a high familial incidence, and the pattern of attack to be strikingly similar from case to case in the family. However, when seen as a sporadic case, and even at times when seen in the family setting, the condition calls for very thorough neurological investigation, including angiography and possibly air encephalography, before its benign nature is accepted.

Apart from the diagnostic problem, hemiplegic migraine also poses a problem in the pathophysiology of migraine. It is now widely held that the altered physiology underlying classical migraine consists of spasm of branches of the internal carotid artery, causing cortical ischæmia, which produces the signs of the aura, followed shortly by distension mainly of the external carotid system, which causes the headache.

Such a mechanism does not adequately explain the picture of hemiplegic migraine. Here the headache may precede the neurological signs, and these may last occasionally for several days. If vascular spasm alone is causing these, some permanent neurological sequelæ would be expected; and these are rarely, if ever, recorded. Two explanations have been offered: (1) the neurological signs are partly due to thrombosis of the finer terminal arteries of the originally spastic vessels, which finally recanalise; and (2) the signs are due not so much to spasm as to cortical œdema, which may be localised or widespread and possibly precipitated by preceding spasm.

The following case is thought worth recording because it draws attention to an unusual syndrome in which the alarming acute phase appears to belie the ultimate good prognosis. The case illustrates well the clinical features of hemiplegic migraine and the strong familial tendency, and angiograms provide evidence of the possible mechanism of the attacks.

## Case-report

A regular soldier, aged 22, was admitted to hospital for investigation of attacks of headache associated with weakness of the right side of his body and inability to speak. Attacks began at the age of 14 and were repeated three or four times a year, until in the past four months he had six attacks. All the attacks were alike and began suddenly with right frontal throbbing headache. About three-quarters of an hour later dots of bright light going round in circles were followed by blurring of vision in the whole visual field of the right eye, not confined to the right homonymous field. However, although the patient stated this quite firmly, later examination during an attack revealed a right homonymous hemianopia, and it seems probable that this was what he had noticed earlier. Within a few minutes his right arm and leg went numb and useless. The numbness was accompanied by pins-and-needles, and the uselessness forced him to unbutton his uniform with his left hand although normally he did this with his right. At that time he could think clearly but could not say what he wished, and other people could not understand him. He then lay down, sleeping intermittently for 5–7 hours, and, after vomiting, found his speech and right limbs were normal again; but he was left with a generalised headache for two days. He was right-handed and on admission was well and symptomless.

*On examination* he was placid, with rosy complexion, slow speech, and moderate intelligence. His blood-pressure at rest was 125/80 mm. Hg. Nothing abnormal was found in his central nervous system, and his body was symmetrical. Radiography of chest and skull was normal. Electro-encephalography showed a diffuse and mildly paroxysmal disturbance without lateralising features. A left carotid angiogram (Dr. P. W. E. Sheldon) showed the arterial branches rather smaller than usual but no other abnormality. The patient had 'Omnopon' gr. $^1/_3$ and hyoscine gr. $^1/_{150}$ three-quarters of an hour before angiography, but spoke and moved normally immediately before it. The nursing orderly who brought him back in the ambulance about half an hour after angiography noticed that he did not reply very well to questions.

*An hour and a half later* he was drowsy but roused on being addressed or on vomiting. His speech was limited to "yes," "no," and "pardon," and he could not say his name. He

responded to simple commands but showed perseveration. His optic fundi had normal vessels and discs. He had right homonymous hemianopia; his pupils were equal and external ocular movements full. He had weakness of the right side of his face, mainly the lower half. Posture was poorly maintained in both right arm and leg, with weakness in the distal muscles of his right arm. Tone was equal and normal, reflexes were symmetrical, the right plantar response was extensor, and the left was flexor.

*Twelve hours after angiography* he was still dysphasic and perseverating. In reply to a request for his name he gave it hesitantly and could not name or indicate the use of a pen.

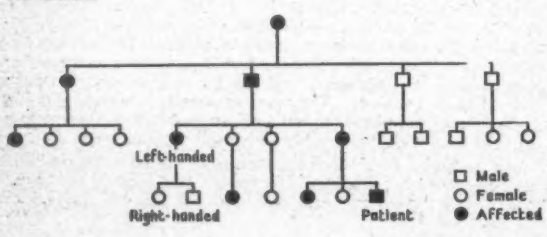
*Twenty-four hours after angiography* he could speak normally and recalled having been shown the pen and having had dysphasia and dyspraxia. He complained of generalised headache, worse in the frontal area and aggravated by coughing; his face was flushed, but he was without pyrexia or neck stiffness. He found that the print on the right side of a page was not quite clear; and, although individual words made sense, he could not read whole sentences; but he placed the hands of a large clock immediately and correctly to show different nominated times, and there was no field defect to confrontation. A slight weakness of the right side of his face remained, and his outstretched right arm showed less well-maintained posture and greater rebound than did the left. His legs showed no difference neurologically, all his tendon-reflexes were equal, and his plantar responses were flexor.

*Forty-eight hours after angiography* his headache had almost disappeared, and he had no difficulty in reading and no abnormal physical signs. He said that this attack was like the ones he usually had.

*A week later* angiography of his left carotid artery showed no difference in vessel calibre between the two sides. Angiography was done at 2.45 P.M. after the usual premedication, and half an hour later the patient complained of right-sided headache and blurring of vision in the right eye. At 3.30 P.M. he could speak normally and asked for some tea, but by 4 P.M. he had aphasia and right-sided signs as before. By 7 P.M. he had vomited and could speak normally, give his name and address, and recount the afternoon's happenings. He had no abnormal physical signs.

*Treatment and Progress.*—His attacks increased in frequency to one a week (previously they had averaged one every three months) while taking isopropyl noradrenaline 20 mg. by mouth at the first warning of an attack, and again if necessary three-quarters of an hour later. On this régime there was a slight reduction in the length of attacks, but this was not very obvious. The noradrenaline was then omitted and he was given phenytoin sodium gr. $1^1/_2$ t.d.s. and was free from attacks for two months. He reduced the dose on his own initiative and, while taking it irregularly, has had no attacks for a further two months.

*Family History.*—His mother, aged 47, was right-handed and in good health and was seen when she visited her son. She described attacks exactly similar to his and said that they began when she was aged 14 and recurred four or five times a year. Examination revealed no abnormality. Her complexion and facial appearance were strikingly like her son's. One of the patient's sisters, aged 13, was right-handed and in good health, had had "bilious vomiting" as a child, and had had only one attack of migraine with motor and sensory loss and aphasia, a year ago. This differed from those of her mother and brother in that the neurological symptoms were bilateral; but such variation in hemiplegic migraine has been recorded. Further inquiry produced from the patient's parents, both intelligent people, the family tree shown in the accompanying figure. In all 9 affected members of the family the attacks were strikingly similar. One aunt was left-handed, and her attacks were of left-sided hemiparesis with aphasia. The condition appears to be inherited through a recessive gene and is not sex-linked.




## Discussion

The occurrence in this patient of an attack apparently precipitated on two occasions by angiography once more suggests that vascular spasm may be a causal factor in hemiplegic migraine, since angiography is known to be accompanied at times by constriction of the vessels injected. The delay, of over an hour in one instance, between the injection of contrast medium and the appearance of symptoms does not necessarily argue against such a mechanism, because the cerebral dysfunction produced must be due to a relative ischæmia resulting from the spasm; and the time of development of a critical level of ischæmia will depend on features additional to the spasm, such as the amount of collateral circulation.

Angiography of both right and left carotid vessels each produced symptoms of left-hemisphere dysfunction. It therefore seems necessary to postulate a local causal factor in the one hemisphere, either making it more susceptible to the effects of spasm of its nutrient vessels or making the vessels more liable to constriction. The calibre of the arteries shown by angiography was sufficiently narrower than usual to call for remark. However, since this was noted equally on both sides it cannot be the basis of any local factor, which, if it be of a structural vascular nature, must be beyond the range of present angiographic demonstration. Some local factor is also suggested by the frequency with which the hemiplegia occurs on the same side both in individuals and in families subject to hemiplegic migraine.

In addition to the mechanism of inception of an attack there is the problem of what pathological process can repeatedly produce a severe local cerebral dysfunction which may last as long as three or four days without leaving permanent sequels. Wolff (1948) noted that, in some patients with prolonged attacks of migraine, hardening of the superficial temporal artery and erythema of the overlying skin followed and persisted for some hours after an attack. Histological examination in one case showed this to be due to œdema in the vessel wall with reduction of its lumen. If this occurs as a sequel to the initial spasm in hemiplegic migraine, it would provide a mechanism for prolonged partial ischæmia of the areas concerned, and also possibly cause a comparable change in adjacent cerebral tissue to the erythema noted over the temporal artery. This might be responsible for the pleocytosis noted in the cerebrospinal fluid during an attack in some of these patients (Symonds 1952, Whitty 1953), but both the kind of cerebral dysfunction which can produce such prolonged but reversible effects and the nature of the local factor remain uncertain. The possibility should be considered that activation of some inhibitory mechanism rather than reduction of normal cell activity may be responsible; the benefit of hydantoinates in some cases of hemiplegic migraine, as in the present case, might argue in favour of this point.

## Summary

A family subject to hemiplegic migraine is reported.

Although the clinical picture at the height of an attack is alarming, the prognosis is good, and none of the signs are persistent.

The implications of such cases for the ætiology of migraine is briefly discussed.

One of us (J. N. B.) has to thank his commanding officer for permission to publish. We are also indebted to Dr. W. Ritchie Russell for the opportunity of studying this case.

### REFERENCES

Clarke, J. M. (1910) *Brit. med. J.* i, 1534.
Dynes, J. B. (1939) *Ibid*, ii, 446.
Symonds, C. (1952) *Trans. Med. Soc. Lond.* 67, 237.
Whitty, C. W. M. (1953) *J. Neurol., Psychiat.* 16, 172.
Wolff, H. G. (1948) Headache and Other Head Pain. New York.

# GUNSHOT WOUNDS IN A HÆMOPHILIC PATIENT

## SUCCESSFUL TREATMENT BY ANIMAL ANTIHÆMOPHILIC GLOBULIN AND SURGERY

G. J. FRAENKEL
M.Ch. Oxfd, F.R.C.S.
TUTOR IN SURGERY IN THE UNIVERSITY OF OXFORD

G. E. HONEY
B.M. Oxfd, M.R.C.P.
SENIOR MEDICAL REGISTRAR, RADCLIFFE INFIRMARY, OXFORD

WHEN a patient with hæmophilia is injured or requires an operation, a situation of great danger has arisen. In accessible lesions, such as bleeding tooth-sockets, hæmostasis can usually be secured for a time by temporary local pressure and a coagulant dressing; but bleeding from larger or inaccessible wounds is likely to persist unless the coagulation defect of the circulating blood can be at least temporarily corrected. In favourable circumstances this may be achieved by transfusion of very large amounts of either fresh blood or fresh plasma (Schiller et al. 1948, Walker 1955), but a much more effective method is to administer an active concentrate of antihæmophilic globulin (A.H.G.). Available human A.H.G. preparations have only a low activity, but highly potent animal material has been prepared by Bidwell (1955a and b) and used clinically by Macfarlane et al. (1954). The level of circulating A.H.G. falls rapidly (Langdell et al. 1955); therefore any surgical operation must be done as soon as possible after an adequate level of A.H.G. in the circulating blood has been obtained.

So far it has not been found possible to prepare animal A.H.G. free from antigenic properties. This usually renders its use impracticable for more than about seven to ten days. This difficulty has been partly overcome by the use of A.H.G. prepared from different species. At present effective A.H.G. in useful quantities has been obtained only from beef and pig blood. Therefore it is necessary to make a plan whereby *all* surgical treatment will be completed and wounds, if possible, healed within the period of effective action of the A.H.G. used. This period is limited to two or three weeks with materials at present available.

As an illustration, it is thought worth while to report a single successful case in detail. The mainstay of treatment was animal A.H.G. prepared as described by Bidwell (1955a and b). This must be distinguished from Cohn's fraction I (Cohn et al. 1946), a human preparation which is often referred to as antihæmophilic globulin in America (Craddock et al. 1948, Wright et al. 1948, Vermooten 1950) and is of very low activity.

### Case-report

A hæmophiliac, aged 22, sustained gunshot wounds on Oct. 6, 1954. He had a family history of hæmophilia, seven members of the present generation being affected (fig. 1). In the past he had had only relatively minor hæmorrhages, none requiring blood-transfusion. On the present occasion a shotgun of 0·410-inch bore was accidentally discharged in a gunsmith's shop, where he was employed as a sales assistant. The shot was fired at fairly close range from behind, causing a deeply grazing injury to his left loin and several puncture wounds scattered over the medial side of his left elbow. He was admitted to the Norfolk and Norwich Hospital under the care of Mr. C. Noon.

*On examination* he had in his left loin a large bleeding wound, which involved the muscle layer, with some loss of superficial tissues. There were also numerous puncture wounds with bruising over the medial surface of his left elbow, where several pellets could be felt underneath his skin.

*Oct. 6:* the wound in the loin was excised, several lead pellets and the cardboard wad were removed, and the wound was packed with gauze. Profuse bleeding followed this operation.

*Oct. 7:* a transfusion of 3 pints of blood was given before the wound was opened again and repacked.

*Oct. 8:* There was again persistent hæmorrhage. A further transfusion of 1 pint of blood was given and the wound repacked.

*Oct. 12:* since there was still profuse bleeding, the wound was sutured and a rubber drainage-tube inserted. Two further pints of blood was given.

*Oct. 16:* since there had been further copious bleeding from the wound in the left loin, 3 pints of blood was transfused. A large clot of blood was removed from the wound and hæmostasis secured by coagulating diathermy. The gentle oozing of blood was stopped with 'Oxycel' gauze. Interrupted sutures were placed over a rubber drain, and the wound was repacked. In the next few days 4 more pints of blood was transfused.

*Oct. 23:* there was further copious bleeding, and the wound was once more packed after removing some blood-clot and arrest of the bleeding by diathermy. 'Coagulen' (Ciba) 20 ml. was given by injection in four doses of 5 ml. six-hourly.

*Oct. 27:* bleeding recurred, and 1 pint of fresh blood was transfused. Another large clot of blood had formed in the wound and was removed. The bleeding points were under-run with sutures, and the wound was packed once more with gauze. A plaque containing 60 mg. of radium was applied over the wound for twelve hours.

*Oct. 28:* treatment was started with adrenochrome monosemicarbazone ('Adrenoxyl') by injection and by mouth, and a pint of fresh blood was transfused.

*Oct. 29 and 30:* on each day 1 pint of fresh blood and 1 pint of stored blood were transfused. The total volume of blood transfused by this time was 20 pints in twenty-four days.

*Treatment with A.H.G.*—On Oct. 30 Dr. R. G. Macfarlane was asked for a supply of beef A.H.G. Since this material cannot be given without special precautions and laboratory tests, members of the pathology department of the Radcliffe Infirmary travelled to Norwich with the necessary apparatus and material. The diagnosis of hæmophilia was confirmed. The clotting-time (Lee and White) was $9^1/_2$ minutes (normal 5–10 minutes), prothrombin-consumption test 67%, level of A.H.G. nil. It was decided to give A.H.G. intravenously and to inspect the wound afterwards. Beef A.H.G. 400 mg. in 15 ml. of distilled water was injected slowly into an intravenous infusion of physiological saline solution, the injection taking about 10 minutes. Soon after this injection was begun, the patient showed a severe reaction, complaining of constriction in the throat, generalised pins-and-needles, and the sensation that he was swollen all over. Objectively his breathing appeared normal, but he was first flushed and later cyanosed. His wound was dry and was bandaged up again. After this had been done, it was noticed that the intravenous infusion had stopped. It was restarted by vigorous "milking down" of the rubber tube, which caused the sudden introduction intravenously of about 3 or 4 ml. of the A.H.G. solution. The patient became rigid and unconscious, and a petechial eruption appeared over his chest and shoulders. He regained consciousness about 15 minutes later.

*Oct. 31:* in the morning profuse bleeding began again, and it was thought that the patient lost about 3 or 4 pints of blood; so 1 pint of fresh blood and 4 pints of stored blood were transfused. It was now that the reason for his severe reaction to the beef A.H.G. was appreciated: seven days previously he had been given injections of 'Coagulen' (Ciba), a preparation obtained from ox platelets. This had sensi-

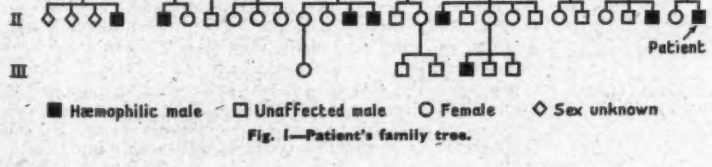



Fig. 1—Patient's family tree.

tised him to ox blood-proteins. An attempt was made to desensitise him with small doses of beef A.G.H., but each subsequent intravenous injection of beef A.H.G. was accompanied by a slight reaction, even when given slowly.

*Nov. 2:* it was arranged to transfer the patient by air to Oxford. In the morning 200 mg. of beef A.H.G. was given intravenously in 40 minutes, with a slight reaction, after which 1 pint of fresh blood and 1 pint of stored blood were transfused. The patient was admitted to the Radcliffe Infirmary under the care of Dr. P. C. Mallam. His hæmoglobin then was 74%, and his plasma-A.H.G. level 14% of normal. The journey by air had been uneventful, and there had been no further bleeding. Another pint of fresh blood was given during that night.

*Nov. 3–5:* there was no more bleeding, and the patient's general condition improved considerably. Daily injections of beef A.H.G. were given, with some reaction during or after each dose. It was thought unwise during this time to disturb either the wound or the dressings. The patient had pain in his left elbow and painful paræsthesiæ in his left hand. A hæmatoma was found overlying the brachial artery in the cubital fossa.

*Nov. 5:* it was apparent that no satisfactory response could be produced with beef A.H.G., probably because the patient had been sensitised to beef protein; so the administration of beef A.H.G. was stopped. Dr. Macfarlane, Dr. R. Biggs, and Dr. E. Bidwell decided to try to prepare A.H.G. from pig blood to overcome this obstacle, and this work was at once started (Bidwell 1955b). This difficult technique was evolved with such enthusiasm and determination that the first small supply of pig A.H.G. was available for testing on Nov. 9. It was the use of this pig A.H.G. that brought the case to a successful conclusion.

*Nov. 6:* at 4 P.M. steady slow bleeding began from the wound. It was hoped that this might cease spontaneously. It did not do so, and it was later found that bleeding, once started, never ceased without active intervention. Although 1 pint of fresh plasma and 2 pints of fresh blood were transfused slowly, bleeding continued.

*Nov. 7:* it was estimated that by noon the patient must have lost 5 pints; so it was decided to arrest the bleeding surgically.

*Operation.*—Special consideration was given to the anæsthetic. It was thought that minimal cyclopropane would be ideal because, to conserve veins, no intravenous injection could be permitted. Induction must be quick and easy, and recovery instantaneous and free from hangover; otherwise nutrition, general condition, and morale would suffer; for we anticipated, correctly, that frequent operations would be necessary. The patient was lightly anæsthetised and his wound inspected. It measured 10 × 10 cm., the edges were about 1·5 cm. deep, and the floor consisted of unhealthy granulation tissue, among which were three definite bleeding points in the line of the intercostal bundles. These were under-run with catgut and covered with human fibrin-foam soaked in human thrombin. The wound was packed with alginate gauze and wool. A wide canvas sling was placed under his waist and the lower part of his chest and kept taut by two 7-lb. weights over pulleys, as is done in the treatment of fractures of the pelvis. He was transfused with 5 pints of blood and 1 pint of plasma.

*Nov. 8:* at 4.45 P.M. bleeding started again. At 8.15 P.M. one of the vessels tied the previous day was found spurting and was again under-run. The wound was repacked as before.

*Nov. 9:* bleeding began at 6.30 P.M.; at 10.30 P.M. this was found to come from the same vessel as before. The delay on each occasion was not due to any hope that the bleeding would stop spontaneously, for by now we knew that it would not. Since at the time no animal A.H.G. effective in this patient was yet available in sufficient quantity, it was necessary to find blood-donors and to give fresh blood before operating. It was thought inadvisable to tie off a vessel containing only unmodified hæmophilic blood, because no effective thrombus forms, and, when the ligature loosens, bleeding starts again. On this occasion hæmostasis was secured and the wound packed as before, but instead of the pelvic sling, which was unsatisfactory, a two-way stretch bandage was applied. This was worse because it quickly rolled itself into a rope at the waist. By next morning it was so uncomfortable that it had to be cut and the pelvic sling reapplied. On this day the first small supply of pig A.H.G. became available, and a skin sensitivity test made with it was negative.

Fig.3—Gunshot wound in back just before grafting.

*Nov. 10:* pig A.H.G. 10 mg. was given intravenously as a test dose and, there being no ill effects, was followed by 200 mg., with no untoward reaction. Fifteen minutes later the plasma-A.H.G. level was only 3·7% of normal. At 8 P.M. bleeding started again and was stopped in the same way as before, after which a one-way stretch Rowden Foote bandage was applied. This proved satisfactory and was used throughout the rest of the treatment. The wound looked much healthier.

*Nov. 11:* pig A.H.G. 1200 mg. in saline solution was given, and the plasma-A.H.G. level rose to 17% of normal. There were technical difficulties in giving the pig A.H.G. intravenously. At first this was suspended in 10 ml. of saline solution and injected slowly. This suspension was so sticky, however, that the piston of the syringe frequently jammed. All further injections were therefore given in a large volume by intravenous drip. Since the patient's plasma-A.H.G. level did not rise as much as had been hoped, it was decided that mixing the pig A.H.G. with fresh human plasma might improve the results. This seemed to be the case. The subsequent daily doses of pig A.H.G. and the patient's plasma-A.H.G. levels are shown in fig. 2.

*Nov. 12:* the patient was tolerating large amounts of pig A.H.G. well. Since this happy state might not last long in view of probable antigenic properties of A.H.G., it was decided that the wound (fig. 3) should be covered with a skin-graft.

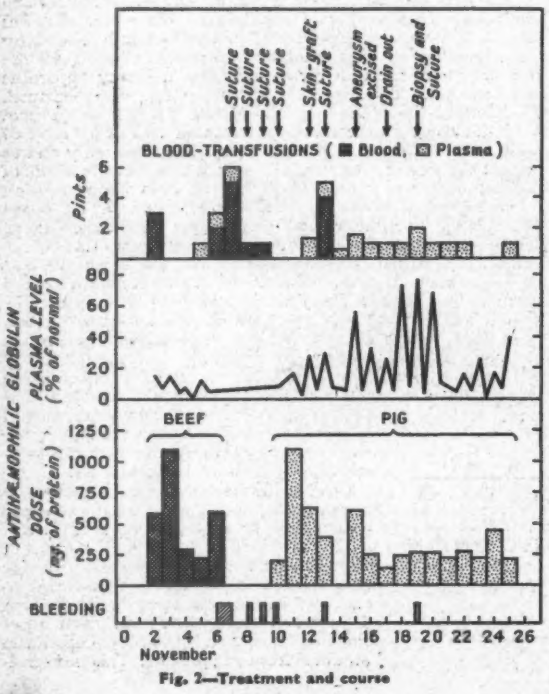



Fig. 2—Treatment and course

Fig. 4—Healed shrunken gunshot wound of back (right-hand rule measures 6 inches).

*Grafting.*—Mr. H. K. McComb cut a large sheet of split-skin graft from the patient's left thigh. The blood from the donor area clotted remarkably quickly, bleeding not being abnormal. Part of the graft was perforated in many places and applied to the granulations on a piece of 'Jelonet' fixed by tie-over sutures placed near the wound margin. Fluffed gauze packing soaked in streptomycin solution was applied and pressure maintained with a sheet of 'Lastonet' glued to the skin. Wool and a one-way stretch bandage completed the dressing. The donor site was painted with human thrombin and dressed in the usual way. The remainder of the split skin was stored in the refrigerator. It was thought that possibly the large amount of pig A.H.G., which had raised the patient's plasma-A.H.G level so little, might have been largely consumed in the formation of the granulation tissue, especially since consistently higher levels were obtained after the wound had been covered with the graft.

*Nov. 13 :* twenty hours after the graft had been applied bleeding started again—from under an overhanging infected skin edge. The blood fortunately had stripped off only about a sixth of the graft. The clot had otherwise accumulated on the surface of the split skin, beneath the jelonet. The bleeding point was under-run and the wound repacked.

*Nov. 14 :* everything seemed at last to be under control, but the patient had more pain than usual at the site of the wound in his left elbow, where signs of a small arteriovenous aneurysm involving the median nerve were found.

*Nov. 15 :* the aneurysm was found to have doubled in size, and the median nerve was further involved. The arteriovenous aneurysm was evidently expanding rapidly and would have to be dealt with. The hæmophilia was reasonably under control temporarily (the plasma-A.H.G. level was 32%), but even this degree of control could not be maintained for long and might break down at any time. It was therefore decided to excise the aneurysm.

*Excision of Aneurysm* (Nov. 15).—With a pneumatic tourniquet in position, the aneurysm was exposed (fig. 5). The median nerve, incorporated in its medial wall, was freed. Numerous venous tributaries were divided and tied with fine thread. The sac was separated from the brachial artery, which had a hole 1·5 mm. in diameter in its wall. A portion of the brachial artery 3 cm. long was resected, and the proximal and distal ends were tied. There was no abnormal bleeding, and the cavity was packed with a piece of human fibrin soaked in human thrombin. The wound was closed round a fine Penrose drain. A very faint radial pulse could just be felt after the dressings were applied, and the hand was pink and warm.

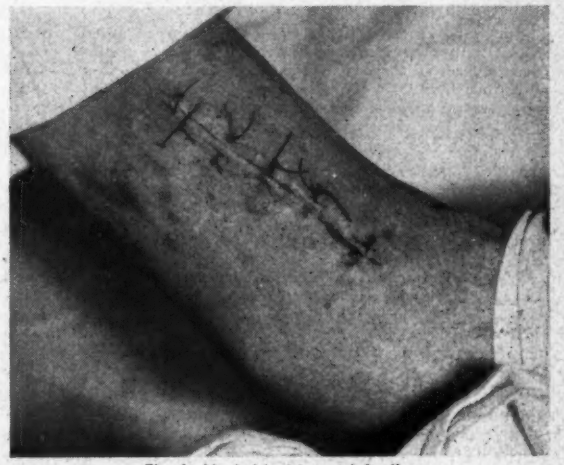


Fig. 6—Healed incision at left elbow.

Fig. 5—Arteriovenous aneurysm at left elbow.

*Nov. 17 :* the drain was removed, and the wound appeared to be healing by first intention. The wound in the back was also dressed. Where the bleeding had taken place on Nov. 13 an area of the graft, about 5 × 1·5 cm., was found to have been rejected. Some of the stored skin was applied to this area. Over the rest of the surface the graft had taken well.

*Nov. 19 :* at 3.30 A.M. blood was seen oozing again from the wound in the back. At 10.15 A.M. this was found to be coming from the same unhealthy overhanging skin margin where the last hæmorrhage had arisen. Excision of this area was thought to be unwise. A biopsy specimen was taken, and the bleeding points were under-run. The specimen consisted of granulation tissue with an artery showing thrombosis, organisation, and early recanalisation. This was the last occasion on which hæmorrhage took place.

*Nov. 20 :* urticaria of the face followed the intravenous injection of pig A.H.G., but next day there was no reaction.

*Nov. 22 :* there was a rigor during the injection; but on the days following there were no ill effects.

*Nov. 25:* all the wounds were dressed. The graft looked healthy, except where there had been hæmorrhage; this area was granulating. The incision in the arm was healed (fig. 6), and the stitches were removed. No further A.H.G. was given after this day. The donor site on the left thigh was dressed for the first time; it was healed and healthy.

*Dec. 2:* the back was dressed again, and it was most remarkable that there appeared to have been no progress whatever in the granulating area since the administration of pig A.H.G. had stopped on Nov. 25. The graft, on the other hand, was consolidating well, and the area of the grafted wound was contracting rapidly.

*Dec. 9:* the back was inspected again: the granulations were grossly exuberant, overhanging the healthy grafted area in a flap 15 mm. wide and 3 mm. thick. These granulations were œdematous and appeared unhealthy. This seemed to support our previous idea that this man was in some way unable to form normal granulations in the absence of A.H.G. and that much of the A.H.G. might have been used up in forming granulation tissue. 'Furacin' ointment was applied to these unhealthy granulations.

*Dec. 11:* the granulation tissue had shrunk and looked much healthier, and more furacin was applied.

*Further Progress.*—There was further improvement during the next few days, and more stored skin was applied to this area on Dec. 15. The rest of the stored skin, taken on Nov. 12 and now five weeks old, was examined histologically and reported to be perfectly normal and apparently viable. Nevertheless on Dec. 20 this last graft also was found to be completely rejected, and the granulations were in their former unhealthy and exuberant state. The area of the granulating unhealed surface appeared not to be contracting at all, although the grafted healed area was still decreasing. There seemed to be no alternative but to treat the granulating wound in the old-fashioned way with daily dressings of furacin, lotio rubra, and crude cod-liver oil in rotation, with daily infra-red irradiation. The granulating area contracted very slowly, and it was not until Jan. 7 that the wound was completely healed (fig. 4). The patient was then discharged home with no residual disability other than the loss of about 10° of extension at his left elbow.

### Comments

The bleeding on Nov. 13, twenty hours after the application of the graft, when a reasonable degree of correction of the coagulation defect appeared to have been obtained, should be regarded as a secondary hæmorrhage, such as is always likely to take place from an old septic wound of this type. It was impossible to maintain a constant effective level of A.H.G. in the circulating blood (fig. 2); so secondary hæmorrhage may be more likely to occur when the A.H.G. level is low.

A contrast is afforded by the excision of the arteriovenous aneurysm. This clean surgical wound, made when there was an effective level of A.H.G., healed normally by first intention, although extensive dissection was required and many vessels were divided.

The manifestations of hæmophilia seem to vary in different patients in a peculiar way which is not entirely understood. It is therefore not altogether certain that these results could always be reproduced exactly in other patients with a different type of lesion.

### Summary

The clinical management of a young hæmophiliac with gunshot wounds is described.

The surface wound was covered with an autogenous skin-graft, and an arteriovenous aneurysm of the left brachial artery was excised.

The success of these operations is thought to be due to the administration of animal antihæmophilic globulin.

The use of this material raises new problems in surgical management, which are discussed.

We are grateful to Dr. P. C. Mallam, under whose care this patient was admitted, for permission to publish these details. In the untiring care of Dr. R. G. Macfarlane, Dr. Rosemary Biggs, Dr. Ethel Bidwell, and their staff the most important part of this man's treatment was carried out, and they gave us advice in the writing of this paper.

It gives us pleasure to thank Prof. T. Pomfret Kilner, and Mr. H. K. McComb and Mr. F. L. F. Innes, who completed the skin-grafting under his direction; Mr. C. Noon, who kindly gave us details of the treatment at Norwich; Dr. R. H. Cowdell who supplied histological reports (not included); Mr. E. L. Tugwell, who took great trouble with the clinical photographs; and many other members of the medical and nursing staff who helped with the treatment of this patient.

### REFERENCES

Bidwell, E. (1955a) *Brit. J. Hæmat.* **1**, 35.
— (1955b) *Ibid*, p. 386.
Cohn, E. J., Strong, L. E., Hughes, W. L., Mulford, D. J., Ashworth, J. N., Melin, M., Taylor, H. L. (1946) *J. Amer. chem. Soc.* **68**, 459.
Craddock, C. G. jun., Fenninger, L. D., Simmonds, B. (1948) *Ann. Surg.* **128**, 888.
Langdell, R. D., Wagner, R. H., Brinkhous, K. M. (1955) *Soc. exp. Biol., N.Y.* **88**, 212.
Macfarlane, R. G., Biggs, R., Bidwell, E. (1954) *Lancet*, **i**, 1316.
Schiller, F., Nellgan, G., Budtz-Olsen, O. (1948) *Ibid*, **ii**, 842.
Vermooten, V. (1950) *J. Urol.* **63**, 30.
Walker, W. (1955) *Lancet*, **i**, 749.
Wright, C. S., Doan, C. A., Dodd, V. A., Thomas, J. D. (1948) *J. Lab. clin. Med.* **33**, 708.

## Medical Societies

### CENTRAL SOCIETY FOR CLINICAL RESEARCH

THIS American society met in Chicago on Nov. 4 and 5. We publish short accounts of some of the papers.

#### Pharmacology of Mecamylamine

Dr. RALPH FORD, Dr. EDWARD DENNIS, and Dr. JOHN H. MOYER (Houston) discussed mecamylamine ('Inversine'), a secondary amine, which is the first known ganglion-blocking agent to be completely absorbed by mouth. Given parenterally to dogs, it produced complete ganglionic blockade at a dose of 0·5 mg. per kg. The cardiovascular and renal hæmodynamic effects were the same as with hexamethonium and pentolinium. Mecamylamine was given orally to 30 hypertensive patients. The average single dose necessary to produce orthostatic normotension was 19 mg. (range 5–40), with an onset of action of forty-five minutes (range thirty to ninety), and a duration of action of twenty-four hours (range eighteen to thirty-six). The intravascular dose required to return the upright blood-pressure to normal was the same as the oral dose, indicating complete absorption. The response was variable from patient to patient, but within the same patient it was reproducible from day to day. Side-effects were constipation, dry mouth, blurred vision, impotence, or muscular weakness; but none of these was nearly so prominent as with the available quaternary ammonium compounds. There was no depression of renal blood-flow or glomerular filtration-rate. Dr. Ford and his colleagues believed that this was the drug of choice in the treatment of patients with severe hypertension.

#### Primary Aldosteronism

Dr. HARRIET P. DUNSTAN, Dr. A. C. CORCORAN, and Dr. GORDON L. FARRELL (Cleveland) reported that renal function was tested in 3 patients with primary aldosteronism due to adrenal cortical tumour and in 1 in whom this condition was strongly suspected. High levels of aldosterone diacetate were found in their urine by differential paper chromatography and by bio-assay. These patients, like Conn's, were unable to form concentrated urine and this defect was, by reference to other renal functions, disproportionately severe. Urines were persistently alkaline. The $T^c_{H_2O}$ was severely negative and, with 'Pitressin,' returned to a normal, positive level. In spite of hypokalæmia, plasma-K clearances were high and in 1 patient approximated to the rate of glomerular filtration. Hypertension was relieved in 2 patients by operation and improved in the 3rd. In 1, there was an unexpected increase in renal vascular resistance and decrease in $C_{PAH}$. However, $T^c_{H_2O}$ in this patient became positive at 3·7 ml.

per minute per 100 ml. of $C_{mannitol}$; plasma-K became normal, with decreased K clearance, and the urine became acid.

The abnormalities in K clearance suggest that aldosterone may act by increasing the degree of ionisation of intracellular K. The renal water defect resembles that seen in the so-called "diabetes insipidus" produced by deoxycortone in dog and rat and by hypokalæmia in the dog. This condition is shown to differ significantly from true diabetes insipidus. In patients with long-continued hypertension, excretion of alkaline urine with a disproportionate reduction in concentrating power was found to be diagnostic of primary aldosteronism.

### Aldosterone in Addison's Disease

Dr. ROBERT M. SALASSA, Dr. RANDALL G. SPRAGUE (Rochester), and their colleagues reported that aldosterone was given to 3 patients with Addison's disease in doses varying from 160 to 800 μg. per day. The effects on electrolyte and nitrogen balances, exchangeable body sodium and potassium, and total body-water were observed. The administration of aldosterone resulted in retention of sodium and chloride, increase in total body-water, and increased excretion of potassium. The abnormal electrolyte and water balances of addisonian crises were corrected. Daily administration of 400 and 800 μg. of aldosterone resulted in retention of sufficient sodium and water to lead to mild œdema of the ankles and face. No significant changes in nitrogen balance were observed, and there was no gross alteration of cutaneous pigmentation. Mild changes in carbohydrate metabolism were noted.

### Continuous Fructose Feeding in Diabetes

Dr. JOHN A. MOORHOUSE (Chicago) said that 8 diabetic patients had been studied to determine the effects of continuous feeding of fructose over long periods. By means of an intragastric tube and standard-speed pump, an adequate and well-balanced synthetic liquid diet was given round the clock. This abolished the usual interprandial demand for calories from body stores of sugar, fat, and protein, and also obviated many of the difficulties of the usual type of balance studies. The diet consisted of a solution of carbohydrate (either glucose or fructose in isocaloric amounts), emulsified fat, amino-acids, vitamins, and minerals. A constant rate of absorption of metabolites was maintained for days or weeks as desired, and fæces were reduced to a minimum. The tolerance of patients for the procedure was excellent.

First, insulin was stopped, and after a control period, continuous feeding was started with either glucose or fructose; all other constituents were kept constant. Periods of glucose and fructose feeding were compared by suitable blood and metabolic balance studies. In diabetes of moderate severity, fructose feeding was accompanied by a well-defined fall in both blood and urine levels of glucose and acetone. A positive nitrogen balance with retention of phosphate and potassium was observed. In severe diabetes, however, fructose appeared to have little or no effect on glycosuria and ketosis. In a patient with acromegaly and insulin-resistant diabetes, ketone levels in the blood and urine fell to normal on fructose feeding, but there was no effect on glucose levels. The observations supported the unitary theory of action of insulin on the cell wall.

### Pantothenic-acid Deficiency in Man

Dr. WILLIAM B. BEAN (Iowa) and his colleagues had studied normal subjects on a diet devoid of pantothenic acid, to which was added ω-methyl pantothenic acid, an antagonist. Burning paræsthesia, muscle weakness, abdominal discomfort, vasomotor instability, infections, and depression developed. Metabolic disorders included histamine-refractory achlorhydria, altered glucose tolerance with prolonged high blood-sugar levels, increased insulin sensitivity, and diminished eosinopenic response to corticotrophin. There were erratic changes in acetylation, and in excretion of 17-ketosteroids and water-soluble vitamins. Severe hypopotassæmia suggested adrenocorticoid dysfunction. Serum sodium, calcium, and phosphorus did not change appreciably. Inability to handle a water load (abnormal Kepler-Power test) appeared. Some of the abnormalities returned to or towards normal when pantothenic acid was substituted for the antagonist in the recovery period. This may have been a true pantothenic-acid deficiency, but the possibility that ω-methyl pantothenic acid is a general protoplasmic poison has not been excluded.

### Selenium Cystine in Leukæmia

Dr. AUSTIN S. WEISBERGER and Dr. LEIF G. SUHRLAND (Cleveland) said that selenium cystine (identical with cystine except that selenium replaces sulphur in the molecule) was effective in low concentrations in decreasing the influx of *l*-cystine into leukæmic leucocytes in vitro. The total leucocyte-count and spleen size rapidly decreased in 2 patients with chronic myeloid leukæmia and in 2 patients with acute leukæmia. Selenium cystine had no effect on 1 patient with chronic monocytic leukæmia. The most striking effects were observed in acute leukæmia. In one patient the leucocyte-count decreased by 200,000 cells per c.mm. within one week and as much as 75,000 cells per c.mm. within twenty-four hours. In chronic myeloid leukæmia the immature granulocytes disappeared more rapidly than mature granulocytes. Responses were obtained in patients who were refractory to other agents. Thus, 1 patient with acute leukæmia who had become refractory to cortisone, aminopterin, and 6-mercaptopurine responded to selenium cystine. This patient subsequently appeared to become sensitive again to 6-mercaptopurine. Toxic manifestations attributable to selenium cystine included nausea, vomiting, anorexia, alopecia, and loss of finger-nails; all these changes were reversible when the drug was discontinued. No hepatic or renal damage was encountered.

### Chlorpromazine and Brucella Endotoxin

Dr. ROBERT S. ABERNATHY and Dr. FRANZ HALBERG (Minneapolis) had noted that endotoxins prepared from gram-negative bacteria, when injected into mice, cause hypothermia, granulocytopenia and granulocytosis, diarrhœa, vasomotor collapse, and death. They demonstrated that chlorpromazine and adrenocorticosteroids gave significant protection against endotoxins. *Brucella melitensis* endotoxin was injected intravenously or intraperitoneally into mice. The leucopenic effect of endotoxin was suppressed, but not abolished, by chlorpromazine. The combination of suboptimal amounts of chlorpromazine and 9-α-fluorohydrocortisone gave added protection. A functioning adrenal cortex did not appear to be indispensable for chlorpromazine protection against endotoxin.

### Experimental Hydrallazine Disease

Dr. PHILLIP COMENS (St. Louis) recalled that hydrallazine hydrochloride ('Apresoline'), a vasodilator drug used in treatment of arterial hypertension, produced a "collagen-like" syndrome clinically similar to systemic lupus erythematosus. Daily doses of 10–12 mg. per kg. body-weight for one to eight months were given to dogs, who lost weight and became weak. Anæmia, leucopenia, hypocholesterolæmia, and hyperglobulinæmia developed. Electrophoretic patterns showed increased β, γ, and $\alpha_2$ globulins with decreased $\alpha_1$ fractions, as compared with normal dogs. L.E. cells and hæmatoxylin-staining bodies appeared. Necropsies and renal biopsies were consistent with lesions of disseminated lupus.

### Diagnosis of Phæochromocytoma

Mr. O. M. HELMER, PH.D. (Indianapolis), described a simple and clear-cut bio-assay of adrenaline and noradrenaline by their action on spirally-cut strips of rabbit thoracic aorta. Only very small amounts of urine were necessary because of an unknown factor or factors in urine which enhanced the contraction induced by adrenaline. The urine from 2 patients later proved to have phæochromocytoma had concentrations of catechol amines 19 to 100 times that found in normal urine. The contraction produced by their urine could be abolished by pretreating the strip with dibenamine, indicating the specificity of the test.

### Vitamin $B_{12}$ and Folic Acid

Dr. JOHN W. HARRIS (Cleveland) described 2 patients with "megaloblastic anæmias," who had severe glossitis, atrophy of lingual papillæ, and cheilosis during therapy with small daily doses of vitamin $B_{12}$; folic acid promptly reversed these deficiency manifestations. He claimed that the administration of small doses of vitamin $B_{12}$ precipitated and aggravated the folic-acid deficiency and believed that this was additional evidence for a reciprocal relation between vitamin $B_{12}$ and folic acid in the metabolic chain resulting in the production of nucleic acids.

# Reviews of Books

## Psychiatry Today

4th ed. D. STAFFORD-CLARK. London: Pelican Books. 1955. Pp. 304. 2s. 6d.

SINCE lay readers are fascinated by psychiatry, it is the duty and opportunity of medicine to use that interest profitably—in particular, to show mental illness as an alarming but intelligible circumstance, and the sufferer from it as a person who can be helped. A good deal of the fascination is a product of fear. In overcoming this, and in learning something of the modern approach to mental illness, the public could do much worse than allow Dr. Stafford-Clark to conduct them. His book is sensible, humane, and accurate, and written in very pleasant English. His preliminary short history of the subject might raise a few medical eyebrows among those who do not know just how black the record of prejudice over mental disorder was—and is. In dealing with psychodynamics he describes, it seems, roughly his own choice among conflicting views. The clinical descriptions are excellent, and well designed to avoid convincing the neurotic reader of his own impending insanity.

The chief weakness of the book is the chief weakness of Western psychiatric thought itself—the lack of effective emphasis on a society or a culture within which the patient lives out his entirely separate and entirely individual mental ontogeny. Neither comparative animal psychology nor comparative social anthropology enter as fully into the picture as they now enter into the study of character-structure. "The patterns of behaviour displayed by members of different societies tend to differ only in so far as they are acquired in response to environmental pressure; in this case the pressure of the cultural or political standards of the society concerned." The word "only" involves a considerable limitation of the resources which psychiatry can exercise in prevention and cure. This may be typical of much clinical thinking, but it is still of ill omen where the writer is dealing with topics such as delinquency, and it limits the prospect of what we might expect from psychiatry in the future.

The lack is even more evident in the section on the "wider implications" of psychiatry, as, for example, in the statements that "Freud and Marx . . . rejected belief in God while clinging implicitly to a system of ethics whose basis they explicitly denied"; and that psychiatry should cease to "provide its own basis for human ethics and values." These remarks seem to pay too little regard to the origins of moral attitudes in human societies, and they weaken the author's (perfectly valid) contention that there is nothing in psychological theory to preclude the holding of religious beliefs.

But it would be unreasonable to ask a book of this size to discuss the phylogeny of moral behaviour, and it contains more than enough excellent expository matter to make it useful and welcome. It is one of the few books of its kind which is really instructive without giving alarm to anxious people.

## Cough Syncope

VINCENT J. DERBES, F.A.C.P., professor of medicine, Tulane University of Louisiana School of Medicine; ANDREW KERR, jun., M.D., assistant professor of medicine, Louisiana State University School of Medicine. Springfield, Ill.: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1955. Pp. 182. 34s.

COUGH syncope is uncommon, but it has been well known for many years, and was certainly recognised by Charcot and probably Sydenham before him. After a bout of coughing the patient falls unconscious (without tongue-biting or a fit) for a few seconds or a few minutes. It is especially prone to attack overweight men with emphysema, who are inclined to excessive smoking, drinking, and exuberant laughter. Falstaff could hardly have escaped an odd syncope or two.

Dr. Derbes and Dr. Kerr have written a full and very readable account of the condition. They prefer the name "cough syncope" to the alternatives "cough syndrome" or "laryngeal vertigo." They deal with the history, symptomatology, and treatment, and discuss possible causes. Their useful review of a fascinating subject includes detailed histories of 35 of their own cases.

## Biochemistry of Autotrophic Bacteria

HOWARD LEES, PH.D., Department of Biological Chemistry, University of Aberdeen. London: Butterworth. 1955. Pp. 112. 21s.

AUTOTROPHIC bacteria obtain their energy either from light or from simple inorganic reactions. There is (as yet) no evidence that they play a part in animal pathology, but their activities in the world at large are so widespread and diverse that they must be looked on as an essential element of life as we know it. Tbis book is written for the student of biochemistry, and the morphology and natural history of these bacteria are incidental to its subject. It is a model of what a specialised textbook should be—lucid, readable, well referenced, and brief. The printing and binding are above the normal standard.

## Surgical Physiology of the Adrenal Cortex

J. D. HARDY, M.S., M.D., F.A.C.S., professor of surgery, University of Mississippi. Springfield, Ill.: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1955. Pp. 208. 42s.

FOR many surgeons the task of keeping up with the complex developments of corticotherapy has been almost impossible, and they will welcome this monograph. Professor Hardy has considered every aspect of adrenal function and its relation to surgery.

The first half is concerned mainly with the effect of operative and accidental trauma on adrenocortical activity; knowledge of this subject appears to be limited to observations which can be interpreted only with uncertainty and surmise. Surer ground is reached in the chapters on adrenocortical hyperplasia and hypercortism, which provide the highlights of the work, being concise and clear. Brevity has perhaps been carried too far in the section on adrenalectomy for malignant neoplasms which occupies only two pages, for here lie some of the most difficult decisions a surgeon has to face, and a fuller discussion of the pros and cons would be of value. The indications and contra-indications in the use of corticotrophin and cortisone in surgery are adequately covered in the final chapter.

## Introduction to Chemical Pharmacology

R. B. BARLOW, M.A., D. PHIL. research fellow, Yale University School of Medicine. London: Methuen. New York: John Wiley. 1955. Pp. 343. 35s.

THE importance of both physical and organic chemistry to the pharmacologist needs no emphasis; and for his part the chemist must give a sympathetic understanding to the problems of the biological scientists, especially when he is trying to make pharmacologically active compounds. It is hard to say whether this book will be more help to the chemist or the pharmacologist. Certainly both should read it, because it does try to bring together two sciences which, though superficially very different, are in fact closely allied.

The chemical structure-action relationships of drugs are adequately dealt with for the groups discussed. The book would have been more useful if greater consideration had been given to the underlying physicochemical aspects of drug action; and in a new edition this might replace the appendix which deals very briefly with some aspects of general physiology. Some controversial parts of the subject are perhaps treated too simply. For example, the results of laboratory tests for analgesic potency can rarely be applied to patients who are in pain, and this makes the testing of analgesics a more difficult affair than Dr. Barlow indicates. Methods of measuring drug action are dealt with briefly. There are excellent bibliographies, and the diagrams and figures are well drawn and informative.

---

**Congrès français de médecine.**—The proceedings of this congress, which was held in Algiers earlier this year under the presidency of Prof. E. Benhamou, have now been published in three volumes. Each deals with one of the main themes of the meeting—*Les thromboses artérielles* (Pp. 534. Fr. 3200), *Le maladies avec auto-anticorps* (Pp. 280. Fr. 1600), *Les nouveaux antibiotiques* (Pp. 392. Fr. 2300)—and each volume may be bought separately. They are published by Masson of Paris.

THE LANCET
*LONDON: SATURDAY, NOV. 26, 1955*

## Coronary-artery Disease

IN the golden period of discovery, the causes of the great fevers were elucidated largely by epidemiological methods. Today we have come to recognise that these methods are equally applicable to non-infectious disorders,[1] and we are hoping that they will reveal the origins of some of the other major sources of morbidity and mortality. More and more attention is being paid, for example, to the epidemiology of coronary-artery disease.

For a long time the vital statistics of all the industrialised countries in Western Europe and North America have been showing an increase in deaths attributed to coronary disease. This increase cannot be taken at its face value: with a higher proportion of elderly persons in the population one would expect a higher proportion of deaths from this cause, and with more general recognition of the disease one would expect it to appear more often on death certificates. Nevertheless, all cardiologists whose experience goes back thirty years or more seem to agree with the vital statisticians that the higher mortality-rates reflect a real increase in coronary-artery disease, and also that young people, below the age of 40, are now affected much more often than formerly. Beside this we have to set the fact that clinicians with experience in the East have long held that the disease is rarer in Asiatics than in Europeans—to an extent that cannot be wholly explained by the Europeans having longer lives. Support for this opinion comes from pathological studies showing that the inhabitants of the Japanese island of Okinawa have little atheroma or coronary-artery disease.[2] In Africa, the post-mortem findings of HIGGINSON and PEPLER [3] at Johannesburg indicate that severe atheroma is far less common among the Bantus than in American and European hospitals. In our present issue Dr. VOGELPOEL and Dr. SCHRIRE, from analysis of electrocardiograms at a Cape Town hospital, conclude that myocardial infarction is likewise less common in the Bantu. Also in this issue, Dr. BRONTE-STEWART, Prof. ANCEL KEYS, and Professor BROCK say that, whereas in Cape Town Europeans the mortality ascribed to coronary heart-disease is similar to that of Europeans in Western Europe and North America, such disease seems to be a rare cause of death in the Bantu, while the Cape Coloured community occupy an intermediate position. In our own country [4] the vital statistics show a well-marked association between social class and the proportion of deaths reported as due to coronary-artery disease, this proportion being much higher in the professional classes than in the manual workers, though the difference appears to be decreasing. Among manual workers, the disease is said to be much less common in Southern Europe than in Great Britain and North America; and, though on such a point statistics can be misleading, at the symposium on arteriosclerosis held in Minneapolis [5] last September PAUL WHITE said that after recent visits to hospitals and clinics in Southern Italy and Sardinia he was confident that there is far less coronary-artery disease there than in the United States. MORRIS [6] points out that the U.S.A., New Zealand, England and Wales, Denmark, and Norway form a series with a descending mortality from coronary-artery disease; and there is also interesting evidence that when Norway was occupied by the Germans during the war there was a considerable decline in deaths from this cause.[7]

An association is apparent between, on the one hand, the prevalence of coronary-artery disease in a population, and, on the other hand, the average level of blood-cholesterol. Thus, KEYS et al.[8] review studies of blood-cholesterol in the U.S.A., Italy, Spain, Sweden, Great Britain, South Africa, and Central America which show that high levels are usually found in persons over 40 years of age in populations with a high prevalence of coronary-artery disease. The data from Cape Town now provided by Professor BROCK and his associates are further evidence of a relation between blood-cholesterol level and such disease. (In this study, as in others,[9] the serum-proteins have been separated on filter-paper by electrophoresis, and there is no doubt that the excess cholesterol is carried in the blood in the β-lipoprotein fraction.) Admittedly, it would be easy to demonstrate that a high mortality from coronary-artery disease is associated with many other features of civilised life—a high prevalence of motor-cars, for instance. But the hypothesis that a high blood-cholesterol is part of the chain of causation gains support from the fact that in patients with proven myocardial infarction the level of cholesterol in the blood is raised [10–12]; and the presence of large amounts of cholesterol in atheromatous lesions is also consistent with a causal relationship.

KEYS [13 14] has shown that in man the level of cholesterol in the blood does not vary with the amount of cholesterol (as such) in the diet, but with the amount of *fat* in the diet. It is well known that the serum-cholesterol level can be rapidly reduced by KEMPNER'S [15] rice diet or by a vegetarian régime,[16] and recently AHRENS et al.[17] have demonstrated that it is also lowered when plant fats are substituted isocalorically for animal fats in human diets. Professor BROCK and his colleagues found wide differences in the intake of fat in their three separate Cape Town communities: a high intake was associated with a high blood-cholesterol and a high prevalence of coronary disease, but the association with plant fats seemed to be much less close.

1. See *Lancet*, 1954, i, 970.
2. Steiner, P. E. *Arch. Path.* 1946, **42**, 359.
3. Higginson, J., Pepler, W. J. *J. clin. Invest.* 1953, **33**, 1366.
4. Logan, W. P. D. *Lancet*, 1952, i, 758.
5. The proceedings of this symposium are shortly to be published by the University of Minnesota Press.
6. Morris, J. N. *Med. Offr*, Oct. 28, 1955, p. 25.
7. Strøm, A., Jensen, R. A. *Lancet*, 1951, i, 126. Strøm, A. Influence of Wartime on Health Conditions in Norway. Oslo, 1954. See *Lancet*, 1954, ii, 1221.
8. Keys, A., Anderson, J. T., Fidanza, F., Keys, M. H., Swahn, B. *Clin. Chem.* 1955, **1**, 34.
9. Oliver, M. F., Boyd, G. S. *Brit. Heart J.* 1955, **17**, 299.
10. Gertler, M. M., Garn, S. M., White, P. D. *Circulation*, 1950, **2**, 696.
11. Oliver, M. F., Boyd, G. S. *Brit. Heart J.* 1953, **15**, 387.
12. Steiner, A. *Circulation*, 1952, **5**, 605.
13. Keys, A. *Ibid*, p. 115.
14. Keys, A. *Voeding*, 1952, **13**, 539.
15. Kempner, W. *Amer. J. Med.* 1948, **4**, 545.
16. Groen, J., Tjiong, B. K., Kamminga, C. E. *Voeding*, 1952, **13**, 552.
17. Ahrens, E. H., Blankenhorn, D. H., Tsaltas, T. T. *Proc. Soc. exp. Biol., N.Y.* 1954, **86**, 872.

From these observations some have assumed that there is no further doubt that coronary-artery disease arises from an excess of animal fat in the diet, and this view has already received wide publicity.[18] We must point out, therefore, that the evidence is still far from complete and does no more than provide an intelligible working hypothesis. Though we know of nothing that directly contradicts this hypothesis, there is much to suggest that there are other factors in the causation of coronary-artery disease, and it would be a cardinal error, at this stage, to ascribe the condition to a single cause. For example, it is generally accepted that women are far less susceptible than men to myocardial infarction, and at the Minneapolis symposium papers were presented by BARR, of New York, and OLIVER, of Edinburgh, showing clearly that œstrogens will lower levels of blood-cholesterol. These levels are also determined partly by thyroid activity; and there is thus good evidence that coronary-artery disease may be in part determined by endocrine factors. Another line of approach was opened by MORRIS and his colleagues[19] when they showed that among London Transport workers the conductors of double-decker buses had less coronary-artery disease than the drivers. This the investigators were inclined to attribute to the protective action of the extra physical activity of the conductor going up and down the stairs; but there is, of course, the alternative explanation that the drivers were under a greater emotional and mental strain. Strain, though of a different kind, might also be the reason for the relatively high prevalence of the disease in the professional classes; but NEWMAN,[20] ARNOTT,[21] and others say that in fact no close association between coronary infarction and emotional stress has been demonstrated. Another possibly important relationship is with hypertension—a much debated subject on which the latest contribution comes from GORDON.[22] Analysing 1490 deaths in persons over 50 in a Greater London borough, he found evidence of hypertension recorded on 18% of all the certificates, and also on 18% of the 287 in which death was attributed to coronary disease. Owing to the uncertainties in the interpretations of death certificates, which GORDON discusses very usefully, too much weight should not be given to these figures, but at least they do not suggest that hypertension is a major contributory factor in coronary disease. In a recent annotation[23] we reached much the same conclusion about tobacco-smoking and coronary atheroma, though we think this needs further inquiry.

Another difficulty is that, as atheroma is a generalised disease, one would expect an increase in coronary atheroma to be associated with an increase in cerebral atheroma; but there does not seem to have been an increase in cerebral vascular disease comparable to the increase in coronary vascular disease. A possible explanation here is that coronary atheroma and coronary infarction are not so closely connected as has been generally assumed; and more thought should be given to MORRIS's analysis of London Hospital necropsy records[24] which suggested that in the past forty years the proportion of people with advanced coronary atheroma has actually diminished. Clearly, for thrombosis to take place within a vessel, there must be some other factor besides atheroma; and we know that a patient can have either extensive atheroma without infarction or infarction with relatively little atheroma. DUGUID[25–27] has produced convincing evidence that an atheromatous plaque can arise within an artery when the endothelium grows out and covers a minute thrombus impacted on the vessel wall, and that such intravascular clots, after attachment, can be organised and subsequently show fatty degeneration. Pathological thrombosis may thus be both the cause and the result of coronary-artery disease.

Any connection between clotting mechanism on the one hand and blood-fat on the other might have considerable significance in linking the findings of the epidemiologist and of the morbid anatomist. FULLERTON[28] has shown experimentally that when there is lipæmia the blood clots more quickly, and he suggests that one factor responsible for the intermittent deposition of fibrin on the arterial intima may be the ingestion of meals rich in fat. Similarly, the investigations of FLOREY[29] and his colleagues[30] at Oxford are beginning to throw light on the relation between blood coagulation and the mechanisms for fat transport. They find that when heparin is injected into the blood-stream of an animal, the plasma is enabled to dissolve chylomicrons which enter the circulation after a fatty meal. In rats, after a fatty meal, the plasma acquires a similar ability to clarify fatty chyle, and this natural clearing action seems to be the same as that which follows the artificial injection of heparin.[31] Perhaps, it is suggested,[32] impairment of this plasma-clearing action of heparin is an important cause of the intravascular clotting in cases of coronary disease. The physiological substance, heparin, may thus have a dual rôle, being responsible both for maintaining the fluidity of the blood and for clearing the chylomicrons after a fatty meal. If we knew more about the chemical factors responsible for the liberation of heparin into the blood-stream and for its utilisation we might understand the mechanisms leading to the thrombus formation and so to myocardial infarction.

Have these discoveries any immediate application in the treatment or prevention of coronary-artery disease? Professor BROCK, when he told the Minnesota symposium about the findings of the Cape Town team, was immediately asked this question. In reply he gave his opinion that people who have had a coronary infarction are well advised to cut down their fat intake. He pointed out, however, that in the traditional diets of persons of European origin from 35 to 40% of the calories are provided from fat, and that severe restriction of fat intake must upset all normal feeding customs. To advise restriction of such a degree would not be warranted, and the physician would be wiser to recommend curtailment of fat

18. *Daily Express*, Oct. 6, 1955.
19. Morris, J. N., Heady, J. A., Raffle, P. A. B., Roberts, C. G., Parks, J. W. *Lancet*, 1953, ii, 1053, 1111.
20. Newman, M. *Ibid*, 1951, i, 1045.
21. Arnott, W. M. *Ibid*, 1954, i, 1251.
22. Gordon, I. *Med. Offr*, Oct. 28, 1955, p. 256.
23. *Lancet*, Oct. 22, 1955, p. 861.
24. Morris, J. N. *Ibid*, 1951, i, 1, 69.
25. Duguid, J. B. *Ibid*, 1954, i, 891.
26. Duguid, J. B., Robertson, W. B. *Ibid*, 1955, i, 525.
27. Duguid, J. B. *Practitioner*, 1955, **175**, 241.
28. Fullerton, H. W. *Proc. R. Soc. Med.* 1955, **48**, 664. See *Lancet*, 1955, i, 543.
29. Florey, H. W. *Proc. roy. Soc.* B. 1955, **143**, 147.
30. French, J. E., Robinson, D. S., Florey, H. W. *Quart. J. exp. Physiol.* 1953, **38**, 101.
31. Robinson, D. S., Jeffries, G. H., Poole, J. C. F. *Ibid*, 1955, **40**, 297.
32. Oliver, M. F., Boyd, G. S. *Clin. Sci.* 1953, **12**, 293.

intake to a level of not more than 30% of the total calories—a recommendation which stood a chance of being followed. Here we must recall that in Great Britain in 1938 fats provided 39% of our total calories and in 1954 the same figure was reached. In 1947, when the fat intake was only 33% of total calories, there was much public dissatisfaction, and in 1950 the British Medical Association's committee on nutrition [33] said that "if the diet is not to become bulky and unsatisfying it is appropriate to increase the proportion to about 35 per cent. as the energy demands of the body rise." Perhaps the committee would now like to have second thoughts?

In conclusion it is clear that we are still a long way from fully understanding the many and complex factors responsible for the heavy loss of life attributable to coronary-artery disease. In discussing ætiology, it is probably important to distinguish between atheroma, a slow degenerative process to which everyone is subject to some degree,[34] and myocardial infarction, which is a sudden affliction of a minority. We still lack precise information about what kind of people get infarctions: are there other important factors, psychological or constitutional? Whatever may be thought about this, Professor BROCK and his colleagues are to be congratulated on the skill with which they have carried out a modern epidemiological survey. The valuable evidence they have collected is consistent with their view that a high intake of animal fat is partly responsible for the high prevalence of coronary-artery disease.

## Who Are the Infectors?

IN the seven years 1947–53 tuberculosis mortality fell more rapidly than at any time in the known history of the disease. Reviewing the statistical returns from 15 countries and the Commonwealth of Puerto Rico, DROLET and LOWELL [35] note a fall in the death-rate ranging from 53% in France to 83% in Iceland; but in 1953 new cases of tuberculosis in four Western countries (United States, British Isles, France, and Germany) totalled 340,416—still a formidable figure—and known cases numbered over 1 million. But, given reasonable opportunities, we can now expect to treat tuberculosis with considerable success in at least 80% of patients, probably more. Once diagnosed, practically all but the recalcitrant and the unteachable soon cease to be a menace to the public health. As we said last month,[36] future infections will therefore arise mainly from the unknown infector, and as the sources of infection become less it becomes more important to search for him. As SIMMONDS [37] pointed out: "As tuberculosis becomes less widespread its significance as an *infectious* disease tends to increase. The need becomes relatively more important when it may find so many susceptibles." The moral is obvious: the decline in tuberculosis calls for an intensified case-finding programme, not a slackening of effort. An epidemiologist [38] has said: "It is wise to regard the present situation not as a permanent advantage over the tubercle bacillus, but as an opportunity to be seized now for intensified preventive measures which will reduce the trend of infection to a point where tuberculosis becomes a sporadic disease or is eradicated."

The significant declines in morbidity as well as mortality have principally been in those countries which have had an intensive case-finding campaign—Denmark and Holland, for instance. In Denmark, before becoming a nurse, midwife, school-teacher, or municipal or civil servant, candidates must produce a certificate to show that they have been found free of tuberculosis by X-ray and other examination. Nurses, teachers, and other school workers are re-examined yearly; merchant seamen, as well as the other services, must also have X-ray examinations yearly; and all prisoners, no matter how short the sentence, are radiographed. In recent years it has become the practice for many public institutions, firms, factories, and so on, to arrange for an annual examination of their staffs, and trade unions have supported this. In Holland, between 1949 and 1954, over 5 million people had mass-miniature radiographs taken, and it is calculated that at least 70% of the population have been examined at least once. In Amsterdam a special effort to survey all those over 50 was 75% successful. As infection in general diminishes, relatively more infectious lesions are likely to be found in older people. In Norway, besides the people covered by the Danish scheme, hairdressers, bus-conductors, taxi-drivers, and food handlers and producers all have a yearly X-ray examination.

There are surely examples here from which we can learn, and which will help in our intensified search for the unknown infector: the waiter with open tuberculosis who coughs bacilli over our shoulders and our food; the "bronchitic" hairdresser with chronic active lesions who spends ten minutes or so spraying organisms from an advantageous height over each customer: the bus-conductor with hundreds of daily contacts within droplet range: the infected old man in the lodging-house who sleeps very close to a great many susceptible young adults. Dr. RYLE [39] has drawn attention to this last danger, and in a letter this week (p. 1136) Dr. MARSH suggests means of dealing with it. So far we have made little organised effort to seek out the active and dangerous sources of infection among these people. X-ray examination related to employment presents certain difficulties, it is true; but is it wise or provident to continue to overlook such potentially rewarding fields of exploration, especially when mass-miniature radiography, useful as it has been in case-finding, is so obviously bowing to the law of diminishing returns? Tuberculosis seems to be spread mainly by a few highly infectious people; we must find these infectors, and we could do so much more readily if certain groups had a regular routine X-ray examination. There is another danger, which may become more evident during the search. An increasing proportion of teen-agers are now tuberculin-negative; and as B.C.G., now and in the future, may well interfere with the value of the tuberculin test, we should see to it that both weapons are used intelligently and as far as possible not allowed to blunt themselves by needless clashing. Our preventive machinery, in fact, must keep pace with the changing needs of the times.

33. Report of the Committee on Nutrition. British Medical Association. London, 1950.
34. Geiringer, E. *Rev. méd. Liège*. 1950, **5**, 614.
35. Drolet, G. J., Lowell, A. M. *Amer. Rev. Tuberc.* 1955, **72**, 419.
36. *Lancet*, Oct. 23, 1955, p. 857.
37. Simmonds, F. A. H. *Tubercle*, 1953, **34**, 314.
38. McFarlan, A. M. *Tuberc. Index*, 1955, **10**, 249.
39. Ryle, A. *Lancet*, Nov. 5, 1955, p. 982.

# Annotations

## "FAIR COMPARISON"

FOR a country like ours, it is essential that the Civil Service should continue to recruit people whose brains and devotion will create and maintain efficiency. In presenting their report on Civil Service rates of pay, the Royal Commission [1] point out that financial considerations are not the sole or even always the principal attraction to the service: tradition, family background, and sense of vocation may all play a part. It will not be efficient, they agree, "unless it contains in all or most classes a certain number of men and women of the highest ability, and a high proportion of at least average ability in the relevant field, all possessing the appropriate qualifications and experience." But they do not think that, either to ensure adequate recruitment or for any other reason, the service should itself set standards for the remuneration of various kinds of worker, "giving a lead on such matters to the country as a whole in order to further a political or social objective"; for to do this would endanger its non-political character. Instead, in the commission's opinion, the aim should be to have a Civil Service "recognised as efficient and staffed by members whose remuneration and conditions of service are thought fair both by themselves and by the community they serve." As an advance on the principles or formulæ previously applied in deciding what Civil Servants should be paid, they propose fair comparison—"fair comparison with the current remuneration of outside staffs employed on broadly comparable work, taking account of differences in other conditions of service." In settling rates in detail, internal or vertical relativities should be used as a supplement, but should never be allowed to override the primary principle.

So that, in the future, fair comparison can be applied with greater accuracy, the commission advise that a fact-finding unit—separate from the divisions of the Treasury which negotiate or decide conditions of pay and service—should be set up to make a continuous and detailed study of pay and conditions. Meanwhile, in making their own recommendations for changes in pay, the commission have necessarily had to adhere largely to the approach followed in the past; and as regards the medical Civil Service these recommendations represent, not surprisingly, a compromise between existing scales and those suggested by the doctors themselves through the Civil Service Medical Officers' Joint Committee. They do, however, preface their figures by the following general statement on the character of Civil Service medical work as they see it, in relation to medical work elsewhere:

> "While it is reasonable in our view to have some regard to the standards of remuneration of general practitioners and consultants in the National Health Service, we think that the type of work and conditions of employment of the practising doctor differ materially from those of most Civil Service medical officers. The typical practitioner is commonly drawn to his profession by a sense of vocation for that profession. The pattern of his working life is entirely different from the more equable conditions surrounding the administrative or quasi-administrative duties, important as they are, of medical officers in the Civil Service. There seems therefore to be a considerable element of self-selection at a reasonably mature age among those doctors who decide to enter the Civil Service rather than to serve the community through the exacting but, to many, more satisfying demands of active practice. Considerable weight should be given in settling the remuneration of this class to the standards obtaining for doctors in salaried employment in the more comparable conditions of local government service and in the rapidly growing field of industrial medicine."

The Joint Committee, for the doctors, had argued that the duties of medical officers require a clinical background, and often clinical acumen. The range of the work, it said, had greatly widened since 1939: for example, the duties in the Ministry of Health involved the examination of difficult and intractable cases occurring in general practice and also the proper influencing of the conduct of the N.H.S. Translating its opinions into money, the Joint Committee took as its first key point the post of chief medical officer at the Ministry, for which it proposed a salary of £6000, based on the income of a part-time consultant with a top merit award. Principal medical officers, it said, should have £3500—corresponding to the pay of a full-time consultant with the smallest merit award. For the medical officer (basic grade) a salary range of £1600–2800 was asked, on the basis of current incomes in general practice. The Royal Commission, however, do not think that the medical officer's maximum need match that of the practitioner with a maximum list, and they propose a salary scale of £1650 (linked to age 35), rising by £75 a year to £1950, and then by £100 a year to £2250. For the chief medical officer of the Ministry of Health they hold that the proper comparison should be with a full-time (not a part-time) consultant, and they recommend that the present salary of £4000 should be raised to £5000—not excluding the possibility that the medical work of the Civil Service will develop to an extent justifying the creation of a post or posts with a salary equal to that of a permanent secretary (for which £6000 is now recommended). On a basis of internal relativities the commission's other proposals include: certain senior posts now with salaries of £2600, £2850, and £3000 to be "broad-banded" at £3250–3750; principal medical officer, £2850; senior medical officer, £2600.

It will be noticed that the Royal Commission's scales offer the least advance to doctors in the basic grade of medical officer, who would rise only from £1595–2100 to £1650–2250. This, however, was to be expected; for a higher rate for this grade was announced only eighteen months ago, leaving the remuneration of the senior grades to be decided later.[2] Whether this starting salary can be regarded as satisfactory depends, in our view, very largely on the prospects of promotion within the service, which have not latterly been good enough. We are glad to note that the commission draw particular attention to the arrangements for special merit promotions recently introduced by the Treasury; for we believe that the future good of the service will depend to no small extent on frequent use of this provision.

## A SECOND CAREER

EMPLOYERS have always been anxious to find the right man for the job; but the inquiry [3] which Mr. F. Le Gros Clark and Miss Agnes Dunne have made for the Nuffield Foundation suggests that they will now have to give more thought to finding the right job for the man. To ascertain the ages at which people retire from work, Mr. Le Gros Clark and Miss Dunne have examined tables for age and occupation compiled in the Censuses of 1921, 1931, and 1951; studying 32 occupations which between them cover about a quarter of the occupied male population. As might be expected, conditions vary. The sedentary craftsman who makes, say, watches or musical instruments remains at his bench long after the signalman has had to leave his box and the coal-face worker his mine. But taking our elderly workers as a whole, more of them retire today in their mid-sixties than twenty years ago, and in 1951 only 48·7% of men aged 65–69 were at work compared with 65·4% in 1931. Better

1. Report of the Royal Commission on the Civil Service 1953–55 (chairman: Sir Raymond Priestley). Cmd. 9613. H.M. Stationery Office. Pp. 238. 6s. 6d.

2. See Lancet, 1953, i, 868, 878.

3. Ageing in Industry. Nuffield Foundation. Nuffield Lodge, Regent's Park, London, N.W.1. 1955. Pp. 146. 6s. 4d. (post free).

pension and superannuation schemes, changing methods of production, and the strains and stresses of two wars are all possible and reasonable grounds for this earlier retirement. But industry can ill afford to lose these experienced workers so soon; and many of them could, with profit to themselves, their health, and the nation, remain at work if they could move to a lighter job. At present some of them find more or less suitable openings for themselves, but the problem is a growing one, and Mr. Le Gros Clark and Miss Dunne believe that about 40,000 alternative jobs of this kind will be needed annually over the next ten years. They think that the time has come for an inquiry into the jobs available and recommend setting up social agencies to help the elderly worker to find a second niche.

## PERCEPTION AND IMPERCEPTION

THE physiological basis of mind has been much studied and considered in recent years: indeed, the physiological (as opposed to the metaphysical) interpretation of mental function has tended to dominate scientific thought. This development was probably inevitable in a field where new clinical and experimental techniques have for the first time permitted reasonably controlled investigation of the activities of the "silent" areas of the brain. To this may be added the effect of the superficially convincing work of the cyberneticists, some of whom have been led to assert that an electronic apparatus will one day be devised to perform all those functions which we regard as the activity of the mind.

But, even if such a machine can be produced, neither this evidence nor the known electrophysiological facts will constitute definitive proof of the philosophical identity of mind and matter. Whichever school one may support, to attempt to resolve the question of mental activity as a problem either in physiology alone or in psychology alone, or to suggest that one approach is more "fundamental" than another, is to create an artificial schism which makes it impossible to interpret cerebral and mental activity satisfactorily. In his Maudsley lecture given to the Royal Medico-Psychological Association on Nov. 10,[1] Sir Russell Brain drew attention to this danger of regarding physiology and psychology as antithetical. As an integrated medical philosopher he used the subjects of perception and imperception as the text for a discussion of the true mind-brain relationship.

We must be careful, he said, not to confuse physical space with perceptual space; our perceptive worlds are private to each of us, though each one stems from our appreciation of a common physical world. Nor must we think that there is any clear distinction between the objective and subjective parts of our private perceptual world, for the information obtained via the exteroceptors is immediately modified by the behaviour of the exteroceptors themselves: the coldness of a stone is identical with a fall in temperature of the fingers. The perceptual world is, then, doubly subjective; for it is a construct of the subject's brain based upon sensory experience from the subject's body.

Turning from the philosophy of perception to the interpretation of various forms of imperception, one sees that acceptance of this reasoning makes for a satisfying interpretation of hallucinations. Because of bodily disorder, a person perceives in his perceptual space things which do not represent objects existing in physical space; but to him they are perceptually real. The many fascinating disorders of the body scheme, including phantom limb, the duplication of limbs, and the various body agnosias are beautifully explained by their status in the perceptual as opposed to the physical world. For the clinical neurologist this concept is of particular value for the rational explanation (though not the cure!) of certain bizarre sensory symptoms which appear to have no organic basis: psychogenic pain, bizarre generalised paræsthesiæ, and relative alteration in size of various parts of the body may be acceptable as modifications of the perceptual body.

Sir Russell had some interesting comments upon the relation between art and feeling. The work of art represents a perceptual form of a physical object embodying the artist's feelings, but at the same time involves the communication of ideas whose reception in turn depends on the perceptual world of the percipient. The fetishist endows an object in his perceptual world with abnormal emotional qualities which are incommunicable. Certain artists may in fact fail to communicate their feelings. The current exhibition of schizophrenic art may justifiably be regarded as an example of these fascinating effects of disorders of the perceptual world.

In drawing the threads of his thesis together, Sir Russell indicated the anatomical bases of the perceptual disorders and propounded a holistic view of nervous activity, indicating that these disorders must take into account the patient's perceptual psychology, emotional background, and past experiences. "The neurological account requires the psychological for its completion," and "even the greatest devotee of the neurophysiological approach to psychiatry will often admit that speaking to the patient is in some circumstances the best method of treatment."

## THE COLLEGE OF GENERAL PRACTITIONERS

DURING its third working year the College of General Practitioners[1] has established itself firmly at home and has extended its influence abroad. The policy of decentralisation, by development of faculties, is being steadily pursued, following the advice of the foundation council that "it will be largely through these regional faculties, and the boards of these faculties, that members will be able to help, and be helped by, the College."[2] Of the 27 active faculties, 5 are overseas; and 4 more overseas faculties are in formation. The next stage is to be the foundation of overseas councils of the college in Eire, Australia, and New Zealand, on the model of the college's council in Scotland. This network of councils and faculties, extending through the Commonwealth and beyond, offers unique opportunities for exchange of ideas and for coördinated work. In different parts of the world general practice has evolved on different lines; yet, unlike the entrant to some specialised fields of medical work, the intending general practitioner seldom gains preliminary experience of practice in other countries. This work of the college may encourage exchanges of practices, and travel in sabbatical years, and thereby reinvigorate general practice at home. To those responsible for the research work of the college, the growth of linked organisations on this wide scale offers peculiar opportunities for studies of comparative morbidity and other epidemiological investigations.

The criteria for membership of the college have become stricter during the year, and a committee set up to study the practicability of an examination has reported its findings. This committee finds that an examination in general practice is practicable and suggests methods for its institution and conduct. A provisional syllabus has been drawn up which lists the clinical, technical, medico-

1. The lecture is, we understand, to be published in the *Journal of Mental Science*.

1. Third annual report of the College of General Practitioners, 14, Black Friars Lane, London, E.C.4. Some details of the third annual general meeting appear on p. 1150.
2. First annual report of the college. *Practitioner*, 1955, 171, suppl., p. 1.

legal, and administrative subjects which a general practitioner in the British Isles may encounter significantly often in his professional life. This list—perhaps the first major attempt to set down in black and white the wide range and scope of the family doctor's responsibility and skill—will inevitably be altered in detail, both in the light of home experience and by overseas councils; but in defining general practice in this way the college has shown that, if ever admission by examination is adopted, those admitted will have to prove their competence not only in the science but in the art of good general practice.

Whatever doubts may have been felt when the new college joined its established seniors in 1952, it is now clear that it has revealed, and is meeting, a need for academic self-expression long latent in general medical practice. Perhaps it is this that gives the council's report a maturity beyond its years, with, at the same time, vitality and energy appropriate to its sturdy youth.

## FAT EMBOLISM

FAT embolism has been known as a complication of trauma for many years, but there has been much argument about how often it occurs and how important it is as a cause of symptoms or death. In 1952 Musselman et al.[1] reported fat embolism in as many as 57 out of 109 patients admitted to hospital with moderate or severe injuries, and they considered it to be a major cause of death in 6 of the injured. On the other hand, as recently as 1951 Whitson[2] argued that fat embolism was not important and suggested that the term be used no longer as a diagnosis. Pathological studies, however, such as those of Robb-Smith[3] and Warren,[4] have established the reality of the condition, and today most people believe that fat embolism is an important, though occasional, cause of death from trauma.

Speaking to the section of orthopædics of the Royal Society of Medicine on Nov. 1, Prof. R. I. Harris, of Toronto, directed particular attention to the clinical recognition of fat embolism. He pointed out that it was not restricted to accident cases, but could follow orthopædic operations,[5] especially when there had been extensive interference with bone-marrow, though sometimes fat embolism followed manipulations involving little damage to bone. Moreover, in a series of thoracic operations, McKeown[6] has recently reported the presence of fat, and sometimes of bone-marrow, in the pulmonary vessels of resected specimens in 14 out of 41 cases; there was no clinical evidence of fat embolism. Professor Harris went on to describe the various "syndromes" associated with the massive entry of fat into the circulation. Sudden death on the operating-table could be due to overloading of the pulmonary circulation with fat. Respiratory distress and fever some days after the operation or accident was more usual. X-ray evidence of consolidated lung often suggested pneumonia; but the true diagnosis might be indicated by petechial hæmorrhages in the skin (particularly in the axilla) or in the retina. It was important to look for these hæmorrhages, which might be caused by breakdown products of minute fat emboli. Professor Harris regarded these hæmorrhages as a more reliable guide than the presence of fat in the urine or sputum. In his experience, pulmonary fat embolism was occasionally associated with severe and extensive hæmorrhage into the lung tissue; and this could then dominate the clinical picture. Cerebral symptoms, usually developing some days after the injury when small vessels became plugged by emboli, were often an important indication of serious fat embolism. Emboli in coronary vessels were also important, and could cause early death after an accident or operation. In the post-mortem examination of these cases, frozen sections, specially stained for fat, from lung, myocardium, and brain tissue, were essential to the proper assessment of the rôle of fat embolism.

Evidence has accumulated to show that non-traumatic fat embolism is possible, probably as a result of chemical alteration of circulating blood-lipids: Kent[7] suggests that diabetes may be a predisposing factor. He compared the lungs of 53 diabetic patients who were examined post mortem with those of a similar group of non-diabetics. Patients known to have had a physical injury within three weeks of death were excluded from each series. 24 of the diabetic group and 11 of the controls showed fat emboli. While most of these emboli were slight and probably of little significance, it is interesting to note that Hedren,[8] in 1916, examining post-mortem material from 60 diabetics, found 1 example of unexplained severe fat embolism, to which death was attributed.

There is little to say about the treatment of fat embolism. The injection of emulsifying agents has not been effective,[9] and is not without risk. The immobilisation of fractures and the use where possible of a tourniquet during orthopædic and other operations reduces the danger of dislodging fat.

## PROFESSOR WYNN'S RETIREMENT

> "To have played an active part in the work of a Medical School and University for a continuous period of sixty years must be an achievement well nigh unrivalled; particularly when the whole career is distinguished by serious contributions to research in its early stages, by remarkable success in teaching later and by fruitful and constructive work in administration during a perplexing period of rapid change and progress."

IN these words the fine contribution made to the life of Birmingham University by Prof. W. H. Wynn is summarised, by the official *Gazette*, on his retirement from directorship of postgraduate studies in the faculty of medicine. Entering the Birmingham Medical School in 1895, Wynn won medals, founded the students' representative council (later the guild of undergraduates), received the degree of M.SC. at the first graduation ceremony of the university, and in 1904, at the age of 26, joined the staff of the General Hospital, which he was to serve as physician for forty-two years. On becoming professor of medicine in 1926, he gave up much of his large clinical practice so as to concentrate on teaching and administrative work in the medical school and university. "He was," says the *Gazette*, "one of the small and resolute group who ensured the success of the plan to build a Medical School and a Teaching Hospital in the closest possible association with the University and he shirked none of the drudgery and controversy that the scheme involved in its development." Recalling also his interest in the problems of infection, his help to the late Sir John Robertson in establishing the tuberculosis service in Birmingham, and his early recognition of the importance of clinical pathology and bacteriology, his colleagues add that he is "no narrow specialist": his studies and experience have been refined "by extensive reading of medical history, by music and the theatre, by generous affection for the young and eager interest in their thought and aspiration." In completing his unusually useful academic career, Dr. Wynn will know that both inside and outside his university this affection is returned.

1. Musselman, M. M., Glas, W. W., Grekin, T. D. *Arch. Surg.* 1952, **65**, 551.
2. Whitson, R. O. *J. Bone Jt Surg.* 1951, **33A**, 447.
3. Robb-Smith, A. H. T. *Lancet*, 1941, **i**, 135.
4. Warren, S. *Amer. J. Path.* 1946, **22**, 69.
5. Peltier, L. F. *Surgery*, 1952, **32**, 719. Schüttemeyer, W. *Zbl. Chir.* 1953, **77**, 1547. Scuderi, C. S. *J. int. Coll. Surg.* 1953, **14**, 508.
6. McKeown, F. *Brit. med. J.* 1955, **i**, 150.
7. Kent, S. P. *Amer. J. Path.* 1955, **31**, 399.
8. Hedren, G. *Svenska LäkSällsk Handl.* 1916, **42**, 933.
9. Glas, W. W., Grekin, T. D., Musselman, M. M. *Amer. J. Surg.* 1953, **85**, 359. Scuderi, C. S. *Surg. Gynec. Obstet.* 1941, **72**, 732.

## Special Articles

# CANCER OF THE FEMALE BREAST, MORTALITY, AND THE MENOPAUSE

ALAN McKENZIE
M.B. Lond., D.T.M. & H.
MEDICAL STATISTICIAN, GENERAL REGISTER OFFICE, LONDON

STUDIES of cancer morbidity are making it possible to construct more accurate age-distribution curves of the incidence of cancer at various sites than has hitherto been possible.

Clemmesen (1951) showed, from statistics compiled in the Danish Cancer Registry in 1942–44, that the age-incidence of cancer of the female breast differed from the age-incidence of cancer in other sites: there was a rapid increase with advancing age up to 45, followed by a decrease between the ages of 45 and 54, and another rapid increase after the age of 55. A similar trend has since been reported from England, France, Switzerland, and America. Typical curves of the relative incidence-rate in four countries are shown in fig. 1.

The influence of the female hormones on the growth and spread of mammary cancer is well known, and the abnormal trend in the incidence between the ages of 50 and 54 "suggests a relationship between cancer of the breast and the menopause; physiologic changes possibly hormonal in origin slow up the rapid rate of increase in cancer of the breast that is found prior to this period" (Dorn 1955).

### Present Investigation

The survivors of 10,025 women with cancer of the breast who had received no previous treatment, were registered under the Cancer Registration Scheme of England and Wales between 1945 and 1947, and had been followed up for five years since the start of treatment, were classified by age-groups.

The prognosis of cancer of the breast being largely governed by the clinical stage reached by the growth when treatment is begun, to assess results it is desirable that each clinical stage be considered separately. Therefore the present series was further classified into the following four stages:

*Stage A:* the primary tumour is freely movable on the chest wall or on contracted muscle; the skin may be involved, but only if it is directly continuous with the tumour; and there is no clinical evidence of invasion of the lymphatic system.

*Stage B:* As A, but with invasion of the lymphatic system.

*Stage C:* the primary tumour has invaded the chest wall or muscle, or the skin is extensively involved; and lymph-nodes may or may not be invaded.

*Stage D:* there is evidence of metastases in distant organs.

These stages derive from the original definitions used at the inception of the Cancer Registration Scheme in 1945. New definitions are now under discussion.

The proportions of cases in the various stages were: A 28%, B 19%, C 42%, and D 10%.

260 untreated patients were excluded from the analysis of stages A, B, and C. The five-year survival-rates were corrected for age by the method of Berkson (1942), all untraced patients being counted as dead. Rates based on less than 100 cases are shown in italics in the accompanying table.

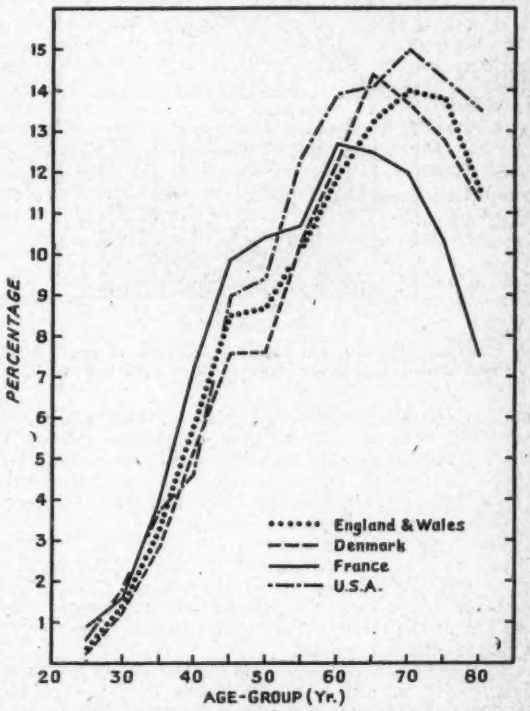



**Fig. 1—Morbidity of cancer of the female breast in different countries by age-groups: England and Wales, 22,174 cases, cancer-registration scheme 1945-49; Denmark, 4579 cases (Clemmesen 1952), cancer-registration scheme 1943-47; France, 4563 cases (Denoix 1954); U.S.A., 3237 cases (Dorn 1944).**

The cancer morbidity-rates presented here are the average annual registration-rates per million of population at risk for cases registered in 1945–49. 22,174 cases were so registered, and an estimate based on the mortality figures suggests that there were at least 50,000 cases in the same period. Except at the very oldest ages, where

REGISTRATION-RATES AND 5-YEAR SURVIVAL-RATES FOR CANCER OF BREAST, BY STAGE AND AGE-GROUP

| — | Age-group (years) | | | | | | | | | | | | | | No. of cases |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 15–24 | 25–29 | 30–34 | 35–39 | 40–44 | 45–49 | 50–54 | 55–59 | 60–64 | 65–69 | 70–74 | 75–79 | 80–84 | 85 or more | |
| *Registration-rates (per million women living):* | | | | | | | | | | | | | | | |
| All cases | *3* | 13 | 55 | 130 | 237 | 346 | 355 | 420 | 489 | 540 | 572 | 567 | 473 | 241 | 22,174 |
| Stage A | *1* | *5* | 20 | 48 | 83 | 119 | 108 | 123 | 138 | 152 | 151 | 140 | 93 | *45* | 6427 |
| Stage B | *1* | *4* | 14 | 32 | 59 | 86 | 79 | 81 | 90 | 88 | 82 | 72 | *52* | *16* | 4198 |
| Stage C | *1* | *3* | 17 | 41 | 77 | 115 | 131 | 170 | 213 | 239 | 277 | 297 | 270 | *156* | 8721 |
| *5-year survival-rates (%) (corrected):* | | | | | | | | | | | | | | | |
| All cases (treated and untreated) | .. | *41* | 35 | 39 | 41 | 45 | 35 | 33 | 36 | 35 | 35 | 36 | .. | .. | 10,025 |
| Stage A (Treated cases only) | .. | .. | *60* | 67 | 66 | 74 | 61 | 59 | 67 | 65 | 69 | 63 | .. | .. | 2765 |
| Stage B (Treated cases only) | .. | .. | *42* | 38 | 46 | 52 | 47 | 43 | 46 | 47 | 48 | *48* | .. | .. | 1841 |
| Stage C (Treated cases only) | .. | .. | *10* | 18 | 25 | 24 | 20 | 22 | 22 | 25 | 26 | 27 | .. | .. | 3924 |

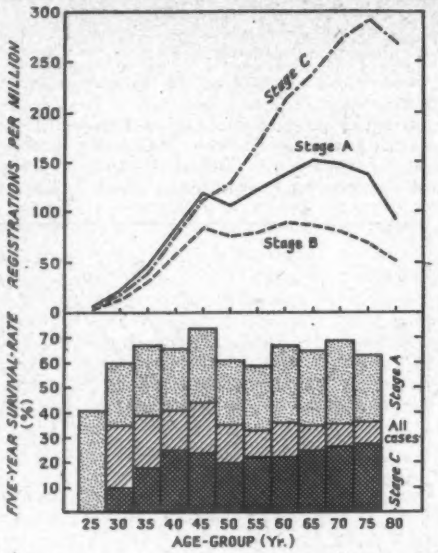



**Fig. 2—Registration-rates and 5-year survival-rates of cancer of the female breast at different clinical stages by 5-year age-groups.**

under-registration is probably greatest, there is no reason to doubt that these rates bear a constant relation to the real incidence-rates, and that at all ages under 75–79 the true rate is about double the registration-rate. (Registration has improved considerably in recent years, coverage now being much greater.)

The results of this analysis are shown in the table, where both the relative incidence indicated by registrations and the five-year survival-rates are given for all cases of breast cancer registered, and for treated cases in each of the three earliest clinical stages separately, in quinquennial age-groups.

The registration-rates in the clinical stages are shown graphically in fig. 2, which shows that the reduced registration-rate between the ages of 50 and 54 occurred only among cancers registered in stage A or stage B. There was no such reduction as regards cases registered when the growth had spread locally beyond the breast or when metastases had developed. Analysis of the survival-rates in the different age-groups shows that, compared with the rates in the age-group 45–49, those in the following decade are considerably lower: for the whole series of treated and untreated cases the survival-rate fell abruptly from 45% at age 45–49 to 35% at age 50–54 and 33% at 55–59.

Among the treated cases the survival-rate fell at the same place in each clinical stage, the fall being greatest in stage A (from 74% at age 45–49 to 61% at age 50–54 and from 61% at age 50–54 to 59% at age 55–59), and least in stage C (from 24% at age 45–49 to 20% at age 50–54 and 22% at age 55–59). After the age of 60 the survival-rate reverts to a higher level but, except in stage C, did not again reach the rate found in the 45–49 age-group.

### Discussion

Bloom (1950) has shown that a larger proportion of tumours of low malignancy are found in the earliest compared with the later clinical stages. This finding supports the suggestion that "the apparently curable stage-I cancers may consist of slowly metastasising tumours, whereas those first seen in the late stages may mostly be rapidly invasive and metastatic tumours whose brief initial stage escaped notice" (*Lancet* 1954).

In the present series the postmenopausal changes in the registration-rate of cancer of the female breast are seen most clearly among cancers registered in the earlier stages. The coincident fall in survival-rates affects all stages but especially the early ones. Both observations suggest that the proportion of breast cancers of low malignancy drops suddenly at this period, and that a growth starting after the age of 50 is more probably of lethal type than one starting immediately before that age. It seems probable, as has been suggested by Clemmesen (1951), that these are "indications of two different kinds of breast cancer sensitive to female hormones to a different degree," with the added corollary from the present observations that the growths which are more sensitive to hormonal influence are of a less lethal type and tend both to grow more slowly and to metastasise later than the less sensitive types of growth.

Analysis of incidence and survival by ten-year age-groups might not reveal the differences shown here, and it is only when very large numbers of cases are collected over a limited period of time that such results can be valid. No single institution could produce the necessary data; it is only possible to do so under a national scheme of cancer registration.

### REFERENCES

Berkson, J. (1942) *In* Carcinoma and Other Malignant Lesions of the Stomach. By W. Walters, H. K. Gray, and J. T. Priestley. Philadelphia and London; p. 467.
Bloom, H. J. G. (1950) *Brit. J. Cancer*, **4**, 273.
Clemmesen, J. (1951) *Acta. Un. int. Cancr.* **7**, 26.
— (1952) *Ibid*, **8**, special number p. 19.
Denoix, P. F. (1954) De la diversité de certains Cancers. Monographie de l'Institut National d'Hygiène, no. 5. Paris.
Dorn, H. F. (1944) *Publ. Hlth Rep., Wash.* **59**, 33.
— (1955) *Amer. J. publ. Hlth*, **45**, 615.
*Lancet* (1954) i, 714.

## COLLEGE OF GENERAL PRACTITIONERS

THE third annual general meeting of the college was held at B.M.A. House on Nov. 19. The president, Dr. William Pickles, was in the chair.

### THE YEAR'S PROGRESS

Presenting the annual report, Dr. George Abercrombie, chairman of council, said that four new overseas faculties had been formed—in Eire (Cork), in Western Australia (Perth), and in New Zealand (Christchurch and Dunedin). An Australian council of the college was being planned. The *Research Newsletter*, under the successful editorship of Dr. R. M. S. McConaghey, had been greatly enlarged, and was now printed and sent quarterly to every member and associate.

The examination committee had published its report. It had shown that if, at any time in the future, an examination was considered advisable as a method of entry to membership of the college, it could be held. Any proposal, however, would have to be passed as a special resolution (of which due notice would be given) by a majority of not less than three-fourths of the votes cast at a general meeting of the college. The question whether or not an examination would be required remained for earnest and thoughtful consideration.

Referring to the reports from the 27 faculties, Dr. Abercrombie said that no-one could read them without a sense of pride and satisfaction that so much had been accomplished by the faculties in so short a time. It had all been done by the initiative of faculty boards in requesting and securing the coöperation of university, hospital, and other authorities. The North Midlands faculty was the first faculty of the college to have been invited by a university (the University of Sheffield) to send a representative to sit on its medical-student selection board.

Reports from the research committee, the undergraduate and postgraduate education committees, and the board of censors, all showed much progress. A register of members of the college who are willing to teach students was being prepared. The response to the questionary on the continuing education of family doctors had exceeded expectations. A suggestion had been made

that next year the James Mackenzie lecture, the annual general meeting, a college dinner, and various conferences might possibly be expanded into a "clinical week" arranged to coincide with hospital postgraduate courses and perhaps with the Medical Exhibition.

Dr. Pickles was re-elected president of the college for 1955–56.

HONOURS

Dr. Abercrombie congratulated Dr. Pickles on his admission to the honorary fellowship of the Royal College of Physicians of Edinburgh, and on being the first recipient of the James Mackenzie medal presented by the council of that college to "the physician engaged in family practice who has made the greatest contribution to medical science." He also congratulated Dr. C. A. H. Watts, who delivered the John Matheson Shaw lecture to the Royal College of Physicians of Edinburgh on Nov. 11.

The Butterworth gold medal was presented to the college by Mr. J. W. Whitlock, managing director of Butterworths, the medical publishers, for an essay on "the influence of home conditions on the physical and mental health of children during their first five years of life." Dr. D. W. MacLean, of Edinburgh, received the first prize, the gold medal, and the *British Encyclopædia of Medical Practice*. Mrs. Beatrice Watts, of Ibstock, Leicestershire, received the second prize, a £20 book token. The subject for the 1955–56 medal and award will be published early in the New Year.

Dr. R. J. Minnitt, of Liverpool, was presented with the Foundation Council award (1955), a small silver gavel on an ebonised base, for "work of the highest merit in the realm of general practice."

THE NEW COUNCIL

The following faculty representatives were appointed to the third college council (1955–56):

| | | |
|---|---|---|
| L. W. Batten | D. L. Crombie | W. S. Gardner |
| H. H. A. Elder | K. M. Foster | J. M. Henderson |
| E. A. W. Marien | R. A. Murray Scott | G. Swapp |
| Annis Gillie | S. Freeman | K. A. Mackay |
| G. Swift | R. Harkness | J. Campbell Young |
| J. C. T. Sanctuary | K. M. Cobban | L. Masterson |
| W. G. Tait | J. N. M. Parry | J. P. J. Little |
| D. Scott Napier | R. Scott | W. A. Conolly |
| R. M. S. McConaghey | | |

(Representatives from certain overseas faculties will be appointed later.)

Twelve members were elected by ballot:

| | | |
|---|---|---|
| G. F. Abercrombie | J. H. Grove-White | F. Charlotte Naish |
| G. O. Barber | H. L. Glyn Hughes | R. J. F. H. Pinsent |
| J. Fry | J. H. Hunt | F. M. Rose |
| I. D. Grant | J. M. Hunter | G. I. Watson |

At a meeting of the new council, Dr. Abercrombie was re-elected chairman, Dr. Rose vice-chairman, Dr. Glyn Hughes hon. treasurer, and Dr. Hunt hon. secretary. Dr. W. V. Howells was appointed as an additional member of council.

## James Mackenzie Lecture

On Nov. 19 at B.M.A. House, Dr. G. O. Barber gave the second James Mackenzie lecture. His subject was Medical Education and the General Practitioner.

Dr. Barber thought there were three qualities that medical education should aim to instil: professional skill, humanitarianism, and organising ability (in that order of priority). Some might question the giving of first place to professional skill rather than humanitarianism; but sound academic knowledge was the first essential. Hence the general practitioner, just as much as the future consultant, must continue to be taught the various branches of medicine and surgery by the specialists. But (and it was a big "but") the student must be given a much broader view of disease than he could possibly get in hospital alone. The conditions which produced illness, and the first symptoms and signs of disease, were all to be observed *outside* the hospital. The most important service that a doctor could do for his patient was to recognise illness at the very earliest possible stage, and it was these early stages that were conspicuously lacking in the teaching of students. On the other hand, academic skill without humanitarianism was a barren thing. Humanitarianism was the sum of all those qualities, apart from professional skill, which one looked for in a good doctor, whether general practitioner or consultant, the qualities you looked for when you were selecting the man to whom you would entrust the health and happiness of your family.

Organising ability was really the application of academic skill to a series of varying situations. General practitioners still had to contend with primitive conditions under which they must set about practising the academic skill they had acquired in hospital; and it was neither fair nor sensible to launch them without some preparation for the enormous change in the technical application of medicine. But, Dr. Barber went on, he had never thought that all this side of general practice should or ever could be taught to the student in hospital. Those responsible for the education of future general practitioners should open the student's eyes to the need for this particular experience and then see that he can get it.

As the demand grew for general practitioners to give students a short glimpse of their work, more and more must volunteer for this duty. "And when we take them, it must be with a very definite idea as to what we are trying to show them." Some students seemed to think that the ordinary stuff of the day's surgery was really a series of trivialities and certificates: it was that impression that had to be corrected. However trivial the patient's complaint appeared, he must never be allowed to go until the question "can this be an early case of serious disease?" had been satisfactorily answered. Moreover, the student should be shown that an accurate knowledge of the patient's heredity and environment was as important as all the diagnostic and laboratory aids. And he must learn to help the patient to "bare his mind" as readily as he will "bare his chest." He must be given a good impression of the relationship between the general practitioner and the hospital. He must never get into the habit later of sending his patients to hospital and then forgetting them.

Turning to the medical curriculum, Dr. Barber said that there was so much knowledge to be imparted nowadays that there seemed a very strong case for teaching mental discipline on subjects which in themselves would be of value to the graduate later on. If this principle was accepted, the preclinical subjects must be pruned right down and only included in so far as they gave the student an idea of the function and the structures of the body and of those substances which affected it. "When we come to the clinical period," Dr. Barber continued, "I want to say with the very greatest of diffidence that the most important thing is to teach our teachers." When every teaching consultant had had a glimpse of the scope of general practice, then there would be little need for this kind of discussion.

Sir James Mackenzie had taught that a proper understanding of health and disease could be gained only by observation of the fluctuations of function in an individual throughout the years; and that this particular side of medicine could be learnt only through general practice. This was a part of undergraduate education which could and should be put into the hands of responsible general practitioners, Dr. Barber declared. It applied to the undergraduate whatever his future branch of medicine, for it would give him a truer picture of medicine as a whole and his particular part in it.

## The First Dinner

At a dinner in Apothecaries' Hall on Nov. 18 Dr. Pickles welcomed some of the friends of the college, and Mr. Dickson Wright, replying gaily for them, declared that but for the grace of God he would still have been a general practitioner himself. Sir Heneage Ogilvie, a supporter from the beginning, spoke of the immense importance of what the college stands for and can do; and Dr. Ian Grant described it as the manifestation of a new spirit in British medicine. To Dr. Pickles, Dr. Abercrombie, and Dr. Hunt, with their colleagues on the council, the company expressed its congratulations.

## GENERAL MEDICAL COUNCIL

OPENING the 191st session on Nov. 22, Sir DAVID CAMPBELL, the president, said that the Special Committee on Public Health, which had been considering revision of the Rules as to Courses of Study and Examinations for Diplomas in Public Health, had found that there was a consensus of opinion that the subjects of instruction prescribed in the existing rules were satisfactory and did not require substantial amendment. There had, however, been criticism, on two grounds, of the *certificate* in public health for which provision had been made for the first time in the rules adopted in 1945. In the first place, little advantage was taken by medical practitioners of the provision enabling them to obtain a certificate in public health, without subsequently proceeding to take the diploma. Secondly, the necessity for arranging, in accordance with the rules, a separate preliminary course and a separate preliminary examination for the certificate had tended to make the teaching of the curriculum for the diploma somewhat less flexible and less effective than it could be if a single unified course were substituted for the existing preliminary course and final course. The revised rules drafted by the committee made no provision for a separate certificate in public health. Apart from the rearrangement of the course which this change permitted, the curriculum proposed did not differ substantially from that provided in the rules adopted in 1945. The revised rules had been generally welcomed by licensing bodies. After certain modifications had been made to meet criticisms of detail, the council adopted the revised rules.

In October the council had issued a list showing the variations in approved hospitals and recognised house-officer posts in Great Britain and Ireland since the second edition of the printed list was published in October, 1954. There was a net increase of 15 in the number of approved hospitals, bringing the total to 742. The number of recognised posts had increased in medicine and its specialties by 38, in surgery and its specialties by 27, and in midwifery by 11. There were also a further 5 posts recognised as conferring experience in both medicine and surgery. The increase in the number of recognised posts in medicine was especially welcome. The total number of recognised posts in the United Kingdom at present was 1246 in medicine, 1519 in surgery and 363 in midwifery; 22 posts provided mixed experience.

## THE NUFFIELD ORTHOPÆDIC CENTRE

Lord Nuffield has given £200,000 for the further development of the Nuffield Orthopædic Centre at Oxford.

The *Times* recalls that the first of all Lord Nuffield's many gifts to medicine was a contribution, nearly thirty years ago, to the repair of the Wingfield-Morris Hospital (then no more than a collection of war-time huts); and since that time he has given the hospital some £220,000, besides establishing the department of orthopædic surgery there, and endowing, in 1938, the professorial chair now held by Prof. Joseph Trueta. The proposal that the hospital with its clinics, and the department with its research laboratories, should jointly receive the name of Nuffield Orthopædic Centre, was made by Trueta's predecessor in the chair, the late G. R. Girdlestone; and it was formally accepted by the Oxford Regional Hospital Board on Nov. 11. The new gift will enhance the value of the hospital as a centre of practice, research, and teaching; but the name of the Wingfield-Morris, which has such happy associations for so many people, will be retained for the present as a sub-title on the notepaper.

# Medicine and the Law

### Coroner's Criticisms Rebutted

A general practitioner was called to a woman patient aged 76.[1] The doctor suspected that she had attempted to take her life by aspirin poisoning and thought she might have taken up to 50 tablets. He arranged for her admission to Hill End Hospital, St. Albans, and told the duty officer there of her medical history. The duty officer, a psychiatric registrar, decided not to wash out the patient's stomach. The patient subsequently died.

At the inquest the coroner was satisfied that death was due to poisoning by self-administered aspirin, and he returned a verdict of suicide while the balance of the mind was disturbed. He expressed, however, some doubt as to whether adequate attention had been given to the deceased on admission, and he wrote to the Mid Herts Group Hospital Management Committee in order that the matter might be "further examined from a medical aspect."

The coroner's letter mentioned that the duty officer did not take a second opinion before deciding not to wash out the stomach. The coroner wondered "whether the fact that this case was admitted late on a Saturday night might not have been a reason for failure to take some further action." He also suggested that the case, being an emergency casualty, should have been sent to the St. Albans and Mid Herts Unit.

The coroner's letter was referred to the Medical Advisory Committee, whose reply expresses grave concern that the coroner saw fit to criticise the medical treatment of this patient.

It would not, they say, be proper for the members of the committee, either collectively or individually, to comment on the treatment of a patient, such treatment is the sole responsibility of the doctor in charge of the case; but there appear to be no grounds for criticising the treatment and no reason why a practitioner of the status of this particular duty officer should have sought a second opinion. The committee also see no justification for the suggestion that treatment is any less adequate on a Saturday night, and they deplore the fact that such a comment was made. The majority of attempted suicides in the area are admitted to St. Albans City Hospital, and the committee agree with this disposal; but the decision in each case must be left to the general practitioner concerned, if necessary in consultation with the hospital.

### Damages for Unlawful Injection

A boy aged 17 has been awarded damages against a doctor who gave him an injection against his will.[2]

In 1953 the boy escorted his younger brother to a chest clinic. The boys belonged to a family where there had been tuberculosis, and the doctor and a nurse considered that a test was necessary on the older boy. The boy refused to submit to an injection but was apparently led to believe that his parents had consented.

An action for damages against the doctor and the East Anglian Regional Hospital Board was heard in Norwich County Court last week. The learned judge said that it was perfectly clear to him that the doctor and the nurse were acting in the best interests of the boy. But even in these days an individual was not forced to submit against his will to some foreign substance being injected into his body just because someone in authority thought it good for him to have it.

"I think the damages for assault must reflect what I regard as the serious impropriety of forcing an injection on the boy in the absence of an emergency" said the judge. "I think the damages are a little aggravated by the fact that the boy was tricked into thinking that his parents had consented. The damages must be more than a simple assessment of the pain of a pinprick."

The judge assessed the damages for assault at 25 guineas. For psoriasis, which the boy alleged had developed after the injection, he awarded £200.

1. *Herts Advertiser*, Nov. 4, 1955.
2. *Manchester Guardian*, Nov. 19, 1955.

## In the Mental Hospital *

# A PROJECT FOR A MENTAL-HEALTH VILLAGE SETTLEMENT

F. HOUSTON
M.R.C.S., D.P.M.
ASSISTANT PSYCHIATRIST, FULBOURN AND ADDENBROOKE'S HOSPITALS, CAMBRIDGE

MANY of our mental hospitals are a hundred years old and belong to the custodial period of psychiatry. If a schizophrenic entered a mental hospital it was intended that he should remain there for the rest of his life, locked up in a ward of 50–80 patients, in dull monotony relieved by an occasional walk round the prison-like concrete courtyard. Is it surprising that the patient became more and more retarded and degraded, the paranoid more paranoid, and the violent more violent? By incarceration we were aggravating the natural progress of the disease.

At last a new era is dawning and the doors of despair are being unlocked: Warlingham Park, Mapperley, Dingleton Hospital, Melrose, and Crichton Royal, Dumfries, have led the way. All sorts of group activities are springing up: physical training, music, art, dancing, and drama are being developed, day hospitals have come into being, admission without formality is allowed in some hospitals, and outpatient clubs are being planned.

But despite the advances made the chronic schizophrenic who has recovered from the acute phase, but is not well enough to return to the ordinary community is still kept in hospital. Before long his family may close their ranks against him, his wife may divorce him, and his chance of recovery is lessened. True, if he is in a progressive hospital, he may work on the farm, in gardens, or in the occupational-therapy department, making carpets, brushes, and baskets. But this is a long way from a normal home life, with the stimulus and incentive of earning a living wage, and the feeling of self-respect and self-reliance it brings.

A change in the existing structure of the mental-health service might serve the interests of the patients as well as lessening overcrowding. Some experiments in other countries and other specialties are encouraging.

### THREE EXAMPLES

The colony of Gheel in Belgium contains approximately 15,000 people in what is to all appearances an ordinary agricultural village. But among the inhabitants 2525 certified mental patients are boarded out from a central observation hospital when their acute psychotic illness is over. They live with the farmer and his family, working on his land, or helping with the housework, and the farmer is paid an allowance for them by the government. This village, however, retains much of the old custodial attitude towards mental patients, and depends too much on charity for the patients and not enough on self-reliance.

In Israel, in the village of Kfar Shaul, there is another mental-health village settlement built on different lines. This is a communal settlement, where all patients are given the maximum amount of freedom. They are employed in constructive occupations such as carpentry, shoe-repairing, and farming. The hospital, which occupies most of the village, has special departments for the tuberculous and the aged. It has 250 beds. This village sells its produce on the open market.

Nearer home the Papworth Village Settlement for tuberculous patients is an organisation which might be copied in the mental-health service.

At Papworth the patients work their own industries, making furniture and motor-car bodies, printing and bookbinding, and producing travel goods for export. They have an annual turnover of £500,000 and compete on the open market, supplying Government contracts and many West End London stores. Though they began in a small way and obtained voluntary contributions, their industries section is now financially sound.

### AN EXPERIMENT PROPOSED

A similar project could be started, as an experiment, at any mental hospital. As a first step, the occupational therapy department could expand its carpentry section, under the guidance of a trained carpenter responsible to the occupational therapist. They could repair all hospital furniture, building their own workshop and benches. They could make furniture for the hospital—lockers, screens, &c.—and could sell their produce, first to the staff, then to the public. Female patients could concentrate on dressmaking: knitting-machines costing £18 or more could be used to make knitwear.

At the end of a five-year period, the aid of a local manufacturer could be enlisted for clothing or furniture, and he would lend more machinery. Second-hand 'Arcon' type prefabs costing £250 each could be put up in the grounds suitably situated for utilising available central heating and electricity. Four to six selected well-behaved patients could be moved into them, or a patient with his relatives. The patients would be paid for their work, at trade-union rates, and, as at Papworth, would pay rent for their prefabs which would cover all revenue expenditure.

In time, if the settlement succeeded, the old central building of the hospital would be emptied into these prefabs, and could be converted partly into the factory building, and partly into an acute treatment centre or ward for sick and senile patients. The village industries, once expanded, could be adapted to build new cottages as well. Admittedly this is looking ahead, for it took nine years at Papworth to reach this stage with the help of a Government grant of £10,000.

The money for a scheme of this kind need not come only from Exchequer funds. In the present shortage of labour other sources would become interested when it was realised what a vast source of energy lies untapped and dissipated in the mental hospitals of this country. A sales manager would be necessary, as in modern times it often costs more to sell an article than to make it.

### MEDICAL PROBLEMS

Living under these conditions a higher proportion of chronic schizophrenics would, I believe, become well enough to return to ordinary life. Among those who could not do so there would be the patient who is still hallucinated, has a few fixed delusions, slight scatter, some emotional blunting, and feelings of passivity, but is nevertheless able to function at a high level. The relatives of such a man might be willing to live in the village with him, knowing that its sheltered environment would help to prevent excited outbursts, and disturbed behaviour.

Selection of cases for such a community would be made by experienced psychiatrists. If domestic conflicts had been the cause of the patient's breakdown, his relatives would be advised against coming to live with him. On the other hand, experience has shown that the families of such patients are often unstable and would themselves

* A group of articles chiefly concerned with the value of active occupation and work for mental patients and the means whereby it is best provided.

benefit greatly from the group psychotherapy they could receive while living in the community. This in turn would help the patient.

Maxwell Jones (1955) often draws members of the family into group psychotherapy, and advises the admission of wife or husband into the social rehabilitation unit at Belmont Hospital. Stengel (1948) found group therapy helpful for schizophrenics. Scheidlinger (1948) holds the re-creation of a family setting to be the primary dynamic element in group psychotherapy.

The patient would reap the benefit of constant psychiatric attention, so that any acute relapse could be prevented, and further separation from the family avoided wherever possible. It is better for the patient to work out his conflicts in a sheltered environment near his family, and learn to accept his ambivalence towards them, than to avoid and repress these conflicts. The families themselves could be employed in the industries section of the village.

Would this emotionally unstable community be a good one in which to bring up children? Obviously not. But, as the fertility-rate of schizophrenics is less than half the fertility of the general population (Kallmann 1939) and schizophrenia is often associated with testicular atrophy (Hemphill 1944, Hemphill et al. 1944), the fact that children must be excluded would not be a serious obstacle to such a project.

The mental-health village settlement could learn from any mistakes made at Papworth in the early days. As most patients would be physically fit, it would have an even greater chance of success than Papworth.

I am grateful to Mr. B. Tallyn, O.B.E., the managing director of the industries section of Papworth Village Settlement, for information about the settlement, which I have visited.

REFERENCES

Hemphill, R. E. (1944) *J. ment. Sci.* **90**, 696.
— Reiss, M., Taylor, A. L. (1944) *Ibid*, p. 681.
Jones, M. (1955) Personal communication.
Kallmann, F. (1939) Genetics of Schizophrenia. New York.
Scheidlinger, S. (1948) Group Therapy Brochure, no. 27.
Stengel, E. (1948) *J. ment. Sci.* **94**, 773.

## Personal Papers

### CHILD AT HOME

As a health visitor I have been troubled by the lengths to which people will go to prevent children from being separated from their parents, even when the home conditions are appalling. I have felt that those concerned often attach a wholly unrealistic importance to "mother love," in the name of which children are left to grow up as best they can in squalid surroundings—neglected, dirty, and often ill treated, with the minimum of supervision from authority. Anything to keep the family together! The article on Separation Experiences and Mental Health by Dr. Howells and Miss Layng[1] will be welcomed by many like myself who had impossible childhoods because adults, relatives, and others hesitated to "interfere."

I am fortunate in being able to remember my childhood clearly, and particularly the important part played in it by the occasional kindness of strangers as well as the sporadic help of relatives. Such help might well come nowadays from the friendship of an understanding adult giving perhaps "day foster care" as suggested in your article.

My parents were separated from the time I can remember, and I was left with mother, who in her despair with life in general progressed from casual drinking to being perpetually drunk. When she drank moderately she became either ferocious or maudlin, both of which states I dreaded so much that I urged her to go on drinking until she became unconscious and there was peace in the house. I would then make a careful round to make sure there were no cigarette-ends left lying around to set the place on fire, prepare myself a meal, and settle down with a book or home-work. This was the usual routine from the time I went to school. My childhood emotions, centred around mother, were confined to hatred, disgust, and pity.

Before I went to school I spent long days alone with a little black cat for company and my toys. Mother usually came in after dark and I would hear her vomiting in the hall. I learnt to go to bed and pretend to be asleep, hoping she would not hear the cat purring at my feet or she would beat us both with a clothes-brush, as she considered cats in bed to be unhealthy. I never told mother, but a neighbour would slip in sometimes when she was out to bring me a cake, stroke the little cat, or admire the way I had set out my toy farm. She always whispered and I knew she was afraid of being caught visiting me. Even now I remember with gratitude the feeling of security associated with her visits—a sane adult in a disordered world. There were others later on—two elderly ladies who used to ask me round and give me cooking lessons; another who let me play in her garden and hid me in the garage if my mother came in pursuit.

My grandparents lived about five miles away in a lovely Georgian farm-house, and once a week or so grandmother would drive round to see us, sigh unhappily, stay about half an hour, and leave me half a crown. I knew she was worried about me but that she did not know what action to take. As I grew older—I must have been about 7 or 8—she told me I could always come to the farm if things got too bad and stay the night. I took full advantage of this, running away quite frequently; and I remember the panic of tearing up the station road. Once in the station all was well; the station-master hid me in his office, denied having seen me if mother had discovered my absence and given chase, paid for my ticket, and put me safely on the train. Soon I would be happily seated in the farm kitchen to which I had been dispatched by grandmother for tea, being mothered by cook and fed sumptuously. Usually mother would follow by the next train or so, and I would hear her shouting angrily at my grandparents; but cook would tell me not to worry, and that I was quite safe with her. She would settle me in an armchair with a couple of cats and *Peg's Paper* and I would feel completely untroubled and secure. The child's capacity for brief happiness is extraordinary: I do not know how I would have managed without these respites from tension and fear. As it is, I am left with a fixation on Georgian houses and cats, no doubt symbols of security and affection. The Georgian houses are less trouble than the cats, who know there is some mystic bond between us and single me out wherever I go for their undivided attention.

Although one can draw no conclusions from an isolated case I do feel sure that children living under emotional strain are helped by any genuine kindness or interest shown in them by an adult, and even more relieved if they can be removed from their surroundings even for brief periods.

My eventual release came when I was 12: father, of whose existence I was hardly aware, decided I should go to boarding-school. I can well remember the relief in being separated from mother, my pleasure in the clean, well-ordered peace of school routine, and the joyful feeling of liberation into a new life.

1. Howell, J. G., Layng, J. *Lancet*, Aug. 6, 1955, p. 285.

# In England Now

*A Running Commentary by Peripatetic Correspondents*

SPACE-TRAVEL will soon be here, and the Ministry of Health doubtless realises that all tourists from Outer Space will be entitled to treatment under the National Health Service. The literature on the flora and fauna of our sister planets suggests that any of our guests who are indisposed will present a problem to the doctor whose knowledge of astronomical pathologies is limited.

Structurally these future visitors offer a series of Morphological Enigma Variations, being (as the Devil remarked of the Ten Commandments) "rather a mixed lot."

Consider first the Beings who are anatomically similar to ourselves, only much more so. Incredibly beautiful and of superb physique, they are grave-eyed and calm-browed, with flowing and strictly hygienic robes and that Fabian outlook which characterises their classless, sanitary, and pale-pink asteroid. They, and their more florid fellow-travellers from the Red Planet, are unlikely to be granted visas for the United States; so many may visit these islands. In any event they will wish to see the London School of Economics and to hear Hadj Bevan's straight-from-the-shoulder talk on the Nationalisation of the Martian Canal System, and his instructions for introducing a 40-hour week to a planet each of whose years, and consequently weeks, is equivalent to $5^1/_2$ earthly ones. After all this they will probably require treatment for confusional states, when their reputation for being physically almost indestructible will invite the most satisfactory surgical excavations.

Many of the other extraterrestrial excursionists will make the creations of Hieronymus Bosch & Breughel, G.m.b.H., resemble a comic strip. Chitinous coverings, palps, antennæ, and edentulous slobbering mouths are fitted to all standard models, while a hankering after human hæmoglobin is distressingly common. Demands for dentures and bottles of blood will cause Parliamentary Estimates to rocket.

Tourists, forty feet high, composed of quartz, and exhaling ammonia gas, will test the equanimity of the Buckingham Palace sentries and cause disquiet in surgery waiting-rooms; but the doctor will only have to diagnose animal, vegetable, or mineral and refer these cases to the Royal Veterinary College, the Ministry of Agriculture, or the National Coal Board.

More difficult as patients will be the Pure Intelligences, existing only as ill-defined clouds of radioactive particles. They will blow every fuse in the house and explode the television set when they attend the surgery for their cyclotron therapy or bottle of Mist. Radio-isotope Co.

In peaceful contrast, the "little people with a shrill, monotonous cry," who emerged from a flying-saucer in France last year, will be indistinguishable from many earthly clients.

The doctor's big moment will come when his space-ship returns from a domiciliary visit and he collects his back-pay and mileage allowance for a journey of several light-years. That should pull out the plug from the bottom of the Central Pool and assure a well-endowed retirement.

* * *

I have been digging out a compost heap, untouched for five or six years. Under the top layers of half-digested rubbish, I came to a pit of wonderful rich brown humus. As I removed this into a wheelbarrow, every spadeful brought back vivid memories. Some small heads and bones, impervious to decay, denoted a period before myxomatosis put paid to rabbit pie. Then came a wish-bone, recalling a New Year's day luncheon party when, despite vigorous tugs and pulling all round the table, it would not break and was thrown out into the refuse bucket. A red rubber ring made me think of hot summer days spent bottling fruit, while surprisingly clean and shiny pieces of tinfoil chocolate-wrapping winked up at me in the sunshine knowing they should never have been there at all. Then came the great find—a table knife, the steel obviously stainless, and the handle barely discoloured. Spurred on by this find, I dug and dug, but the rest was just a mass of perfect mould. I thought how strange it is that time alone, aided by 'Adco,' should transmute such unattractive horrors—fish bones, meat innards, every form of fruit and vegetable peeling—into the delicious sweet-smelling earth ready to feed the roses for next summer's flowering.

* * *

You can see we are a dull lot in our department if you come and look at our animal-house. There are a few mice, a number of sinister-looking variegated rabbits, and an altogether excessive accumulation of plain white rats. No tropical fish, no snakes, no piglets. In other departments one can entertain visiting firemen for hours merely by taking them to see the baboons or the porcupines, but the entertainment rating of our animal-house is nil.

The whole thing is a great trial to our patient and industrious administrator. In spite of a number of years spent in tracking down mysterious leaks of D.C. current, distributing cleaning materials, cataloguing the Professor's library, and reprimanding our recalcitrant students, she retains an incurably romantic disposition in respect of this matter of animals. When we called on her the other day to ask about our dirty windows we found her just finishing a telephone conversation. "Well," she was saying, "if you don't know when the frogs are going to come in, could you at least put me on the waiting-list for salamanders?" She put down the telephone and showed us a catalogue she had received that morning. "Why don't you try something different?" she asked, and we thought we could detect an incipient curl of the lip. It was indeed a stirring catalogue. We reluctantly rejected the Elephants (each £750 F.O.B. Singapore), the Tigers (each £325–£350), and the Black Panthers (£325), all in Splendid Health and Condition, and our eye wandered down through the Slow Lories, the Binturongs, and the Ursine Tree Kangaroos (each £40) to the Black Headed Munia and the Green White Eye Brows (each 10s.). We considered a pair of Red-rumps at £5 or a pair of Twentyeights at £14 10s., and noted with interest that the prices of Lions, Giraffes, Zebras, Hippopotami, and Shetland Ponies were all subject to market fluctuations. Finally we settled for a couple of Turtles for Aquariums (small)—each 5s.

But we fear that our enterprising order has done little to improve matters. As we left, the phone rang again. It was pathology, wanting to borrow some mice. Our administrator was quite sharp with them.

* * *

Our M.O.H., a regular peripatetic, usually secretes a few pearls of wisdom in his annual report on our state of public health. In the volume for 1954, under the section on clean food and its handling in house and warehouse, we read: "Every link in the chain of infection must be remembered; that chain hangs as a symbol over every water-closet in the district."

Ours has a handle.

* * *

It had been a long holiday and we had just enough money left to see us home. We stopped to fill up with petrol for the last time. "Nine gallons should be enough to get us there," I said, "and I can do it with a shilling left over." "But," said my wife, "we must have bread—and milk—for tomorrow's breakfast." When we had laid aside enough for these necessary supplies, we found that we could only manage eight gallons of petrol. So we had a whip round and recovered the pocket money from the children. We put in the nine gallons and set off. The journey was unusually peaceful. It took me some time to realise that this was because there were no intermittent demands for ice-cream. The children knew that it was no use asking.

It seems that unwittingly we have scored a psychological bull's-eye. Since we arrived back home, the children have become money-conscious. Instead of "can I have an ice, Mummy?" it is now "can we afford any ices today?"; and the two older children have separately inquired: "Where does the money come from that Daddy gets out of the bank?" Even the five-year-old seems to be enlarging his wordly horizon. "Daddy," he asked, the other day, "are income-tax a special kind of tin-tacks?"

* * *

What is a skean dhu?

A pigeon that goes to Switzerland for its Christmas holidays.

# Letters to the Editor

## AN INCOMPLETE VICTORY

SIR,—Dr. Anthony Ryle has raised a very important question in his letter of Nov. 5. If the problems of tuberculosis control are to be solved successfully they must be tackled much more energetically than hitherto. One of the major difficulties is the "chronic infector pool" and many patients who came into this category are to be found in common lodging-houses and reception centres throughout the country. According to the National Assistance Board's 1954 report the night attendance for hostels under the Board's care varied from 2402 in February to 1776 in July.

In Camberwell there is the largest reception centre in Great Britain. The average night attendance varies between 603 in February and 410 in July (1954 figures). Because Dr. J. C. Hewetson, visiting medical officer, was worried about the incidence of tuberculosis among the men who reported sick to him, it was arranged for one of the South East Metropolitan Regional Hospital Board's mass X-ray units, under the direction of Dr. J. M. Morgan, to carry out a survey. In May, 1955, 175 men were examined, and 13 new cases of pulmonary tuberculosis were found in men over the age of 45. It was possible to arrange for the admission to hospital the next day of those in need of treatment. This is a prevalence of 87 per 1000. It should be noted that the prevalence for the same age-group among the general population in the County of London is 2 per 1000.

It is probably not possible to calculate from national figures the total turnover of new men going through the hostels but it is thought to be high, since a large number of the men are immigrant labourers (mostly Irish), men only temporarily out of work, or who may be having difficulties with their families or are in some way under duress, and go to these reception centres only for a short time. These patients are usually younger people and if they acquire infection from the older chronic patients they may well take their infection either to their new job or equally important, back to their home.

I would suggest that there should be a national Mass X-ray Day for the inhabitants of these reception centres, hostels, and common lodging-houses: the actual date would *not* be made known to the inhabitants, otherwise the hostels might well be empty! If all the directors of mass X-ray units would coöperate, a survey could be carried out on these men on a given day, preferably in the winter, when the population in these dwellings is high. In this way some idea of the incidence of disease in this particular population could be obtained. Furthermore, coöperation could be obtained from owners of the common lodging-houses which are maintained under licence. Even if it were not possible to examine the inmates it would be possible to obtain a "bed return" of the day on which the survey was made in order that further estimates could be made of the population at risk.

Patients in a different type of institution, the Rowton House, would be more difficult to examine because separate accommodation is provided. These buildings are licensed as private hotels but if the coöperation of the superintendents were invited it would probably be forthcoming.

Once the men with evidence of tuberculosis have been identified, seen by the chest physician, and, if necessary, notified, it should be possible to compile a register which could be circulated to all chest physicians in whose area there are lodging-houses and hostels. This register would in no way be a breach of confidence because it would be circulated to doctors only. It would then be for the chest physician to make what arrangements he felt were necessary to ensure that any patients on this register should be referred to him if they visit the lodging-houses in his area. It would soon become obvious to these men that the services of chest physicians were available to them and, if our experience in Camberwell is any guide, it would probably be found that they are quite willing to accept treatment and stay in a sanatorium until they have been made much better. Even if they do not stay for long, it would probably be possible to give them outpatient chemotherapy.

If the disablement rehabilitation officer visiting the sanatorium works in close liaison with his opposite number where the lodging-houses and reception centres are situated, it should be possible to salvage a number of these men and get them into gainful employment. It must be admitted that the men, who for various reasons, have been in reception centres only for a short time, are more likely to respond than those who have been circulating in these institutions for a number of years. It must be remembered that the older men occasionally use public transport and certainly go to cheap restaurants and cafés for their meals.

There is also a need for increased special hostel accommodation or segregation within a hostel for men who are known to have active tuberculosis. If at the same time it is possible to find work for them in some form of sheltered workshop, then the draining of the chronic infector pool could begin.

Camberwell Chest Clinic, London, S.E.5. KENNETH MARSH.

## CONSULTANTS IN DERMATOLOGY

SIR,—Very many senior registrars with higher medical qualifications and general medical experience have in addition received a full training in dermatology as recommended by the Royal College of Physicians and have for some few years been awaiting the consultant posts for which they are so well fitted and to which they are entitled.

It is disturbing that there should still be delay in creating the number of consultant posts necessary for a reasonable service to the community, and it is improper that posts should be advertised as including one or two sessions in venereology, so excluding properly trained dermatologists. It is, however, more disturbing to learn that some regional boards are considering the appointment to consultant dermatological posts of consultant venereologists employed by these boards but with insufficient work in venereology.

If this manipulation of posts by the administrators in the health service is allowed thus to interfere with the establishment of proper medical services it is a matter of grave concern to the public. The community is entitled to be served in this large and important specialty, as in other branches of medicine, by persons who are properly trained and experienced. On the other hand those senior registrars who have devoted this time to a prolonged and proper training are entitled to a fair deal in consultant appointments.

The quality and pattern of services in a specialty are fixed for twenty or thirty years by any particular appointment today. The harm and disservice which may be done to medicine by irregular and improper appointments cannot be exaggerated.

It is to be hoped that the Minister will not countenance such practice by regional boards in spite of the laudable desire to allow boards reasonable autonomy.

Leeds. JOHN T. INGRAM.

## BREAST CHANGES IN FIBROCYSTIC DISEASE OF THE PANCREAS

SIR,—I am anxious to discover whether any of your readers have found a swelling of the breasts or pigmentation of the nipples in cases of fibrocystic disease of the pancreas, since I have now had three such children between the ages of 3 and 5 years.

In the first child the nipples were pigmented a deep brown colour similar to that seen after the administration of stilbœstrol, but there was no chance that this drug was involved. The other two cases showed less deep pigmentation, but there was some enlargement of the breasts. When I saw the first patient I thought that these breast changes might be the result of the prophylactic aureomycin which he had been receiving during the winter; but stopping this drug caused

no dramatic change, and the next two children were not receiving this drug at the time when the breast changes appeared.

I inquired from Lederle Laboratories Ltd. whether they had received any similar reports with this drug, and found that they had not. The only possible connection they could suggest was the finding of light sensitivity in some patients receiving aureomycin during a trial of its value in epilepsy.

Dr. Eric Stroud, of the department of child health in Cardiff, has shown me an infant of 6 months who had a similar enlargement of the breasts, and he suggested that the condition might be related in some way to the known abnormality of glandular tissue in fibrocystic disease of the pancreas.

Plymouth. HUGH JOLLY.

## USE OF CORTISONE

SIR,—I feel that the recent decision of the Ministry of Health to allow the free prescription of cortisone and hydrocortisone is a somewhat unwise one at present.

I do not of course deny the benefit conferred by these substances to patients whose illnesses demand their use; but in the present state of our knowledge I can only conclude that there will be a great danger of irresponsible prescribing of these drugs. In addition to their specific uses in Addison's disease, hypopituitarism, after bilateral adrenalectomy, and in other forms of replacement therapy, they are also very efficacious, albeit only symptomatically, in a large number of other conditions. These are illustrated in your timely leading article and in Dr. Bayliss's article last week.

The side-effects of cortisone and allied substances are multiple and may have serious consequences, but I do not in any way suggest that these are out of the control of the general practitioner. He is often the first to recognise the initial symptom or sign of potentially dangerous maladies, but these may be absent in those receiving cortisone.

If cortisone is freely prescribable many sufferers from disabling but non-fatal conditions will demand it from their doctors. The doctor will know that their symptoms will be relieved by it, and it will be hard to refuse.

In my opinion the diagnosis and treatment of those patients for whom cortisone is indicated should continue to be under the control of hospitals. There are relatively few such patients, and in any case they need to have occasional hospital consultation to assess progress and the development of side-effects, if any.

In conclusion, Sir, I would suggest that the decision to release cortisone for general use is at present an unfortunate one from both pharmacological and human viewpoints. Until we know more about the uses of this drug, the safer alternative would be to make it available to all hospitals.

London, N.W.11. D. S. NACHSHEN.

## PREVENTION AND THE PRACTITIONER

SIR,—For the past four and a half years I have practised the precept mentioned at the end of your annotation last week. I have eliminated ordinary surgery attendances and have done all my work in the homes of my patients. I have a small list spread over a wide area of country, and do my own dispensing for three-quarters of my list.

Messages arrive in various ways, but the great majority come in during my surgery hours, when it is known that I can answer them personally and often say when I am likely to arrive at the house. Urgent calls, of course, come at any time and take precedence over routine work. Not much extra mileage is involved, because the house-bound who are to be visited generally live near the potential surgery-attender.

The scope of my work is not limited in any way, and includes full domiciliary midwifery. The effect of health education, so easily carried on in the home, is most clearly shown by the steady decline in items dispensed each month, and in the elimination of placebos and nostrums from my drug order.

Since I am single-handed and unable to afford ancillary help, administration is run on up-to-date office lines. I have two breaks each year, one of them educational, and the locums who have come to do my work have found the scheme easy to run.

Hutton-le-Hole, Yorks. RICHARD N. THEAKSTON.

## MYASTHENIA GRAVIS AND HYPERTHYROIDISM

SIR,—Dr. Tabachnick (Nov. 12) discusses the possible ætiology of myasthenia gravis and the relation of this condition to hyperthyroidism. He concludes from his experimental data that the most acceptable hypothesis is diminished synthesis of acetylcholine. We should like to point out that this view is not compatible with our own findings using decamethonium in myasthenic patients.

Briefly, we found that patients with mild and localised myasthenic weakness show diminished sensitivity to decamethonium, but those with generalised signs do not have this tolerance. Furthermore, whereas in healthy persons decamethonium produces a neuromuscular block by depolarisation, in myasthenic patients the block is of the "dual type."[1] Zaimis[2] has described a similar type of neuromuscular block in animals.

These findings suggest that the underlying dysfunction in myasthenia is an alteration in the manner of response of the motor end-plate to acetylcholine, rather than any change in the amount liberated at the nerve-ending.

St. Thomas's Hospital, London, S.E.1. H. C. CHURCHILL-DAVIDSON.

Royal Free Hospital, London, W.C.1. A. T. RICHARDSON.

SIR,—Dr. Tabachnick, in his most interesting letter, makes two suggestions which do not conform with experiences in clinical anæsthetic practice. Furthermore, I believe that he has inadvertently misquoted MacLean[3] as saying "that hyperthyroidism lowers the raised cholinesterase level of myasthenia gravis." MacLean simply postulated that "in hyperthyroidism acetylcholine is present in excess owing to the absence of adequate amounts of cholinesterase." MacLean did not state that the cholinesterase level was raised in myasthenia gravis; and the evidence suggests that the level is normal in this condition.[4] My own experience, and that of others,[5,6] suggests that in hyperthyroidism the majority of patients have a raised, not lowered, cholinesterase level.

Dr. Tabachnick suggests that hyperthyroidism leads to a relative overabundance of a depolarising substance, and that, hence, these patients might be sensitive to the effects of depolarising relaxants; but in practice I have found that in hyperthyroidism patients are resistant to the effects of at least one depolarising relaxant—suxamethonium (succinyldicholine).

All these facts can be reconciled in one hypothesis, though, like others, this will doubtless be open to criticism:

If in hyperthyroidism there is a raised production-rate of acetylcholine (as Dr. Tabachnick shows may well be possible), then the rise in cholinesterase levels which I and others have found may be secondary to this; but the raised cholinesterase level may still incompletely compensate for the increased acetylcholine production. As MacLean remarks, the excess of chemical transmitter then present might produce (by persistent depolarisation) an incipient or actual neuromuscular block, and consequently might be the factor responsible for the muscular fasciculations, tremors, and myasthenia-type weakness in hyperthyroidism. Theoretically this thyrotoxic myopathy should be cured by anti-thyroid treatment and should

1. Churchill-Davidson, H. C., Richardson, A. T. *J. Physiol.* 1953, **122**, 252.
2. Zaimis, E. J. *Ibid*, p. 238.
3. MacLean, H. C. S. *Lancet*, 1954, i, 1296.
4. Maclean, B., Wilson, J. A. C. *Ibid*, p. 950.
5. Antipol, W., Tuchman, L., Schifrin, A. *Proc. Soc. exp. Biol., N. Y.* 1937, **36**, 46.
6. Lehmann, H. *Proc. R. Soc. Med.* 1955, **48**, 624.

not respond to neostigmine.[7] In those cases where neostigmine has been of benefit,[7] the mechanism may be akin to the paradoxical reversal of suxamethonium by neostigmine in anæsthesia, which I have noted previously,[8] and which has since been confirmed by others.[9]

If this state of excess acetylcholine balance, which presumably is present in hyperthyroidism, is superimposed on true myasthenia gravis (where conditions leading to a relative lack of acetylcholine appear to be the underlying cause), then normal balance may be resumed. Hence the alleviation of true myasthenia gravis by hyperthyroidism, and the worsening of the myasthenia by anti-thyroid treatment.

By this argument, in fully compensated patients with hyperthyroidism (i.e., where the rise in acetylcholine production is matched by a secondary rise in cholinesterase) the balance would be preserved. Consequently such patients would be unlikely to show symptoms of acetylcholine excess, nor would the condition alleviate true myasthenia gravis. Is this the explanation of the considerable divergence of findings as regards the effects of anti-thyroid treatment on the signs of myasthenia gravis in proved cases of combination of the two diseases ?[4]

Dr. Tabachnick's further postulate—that hyperthyroidism should be associated with a resistance to depolarising relaxants—is not borne out in practice with suxamethonium, probably because the common associated rise in cholinesterase levels is responsible for the rapid hydrolysis of the drug. I have no knowledge of the resistance of thyrotoxic patients to decamethonium, a drug which is not hydrolysed by cholinesterase; and it would be of interest to know what others have found in this respect.

Portsmouth. R. J. HAMER HODGES.

SIR,—We have read with great interest the informed comments made by your correspondents on this subject. Certain points appear to call for replies, either in amplification of our earlier views or in relation to new matters raised. Dr. Tyndel (Nov. 12) has brought up a nice semantic point in reconsidering the implication of the word *gravis*. The historical background to the term is beautifully elucidated in his letter but we are sure that he will agree that usage is one of the most potent forces in philological evolution and that current usage does attribute to the adjective gravis a serious prognostic import, quite independent of any archaic diagnostic derivation. The persistence in some textbooks of psychiatry and neurology of a warning against the confusion of myasthenia with psychogenic symptoms or even malingering is very reasonable but irrelevant to the semasiological issue.

As to the use of corticotrophin. Our reading of the literature has led us to the conclusion that not even the term "controversial" need be applied there, and since we did not ourselves employ it in the treatment of our cases we could offer no first hand comment on a form of therapy which had proved largely ineffective in the opinion of others.

Dr. Tabachnick discusses the possible relationship between myasthenia gravis and hyperthyroidism. This subject has interested us profoundly and we hope shortly to report our clinical experiences. Meantime we should like to point out that not everyone can agree with the assertion that when hyperthyroidism and myasthenia co-exist, there is no muscular weakness. If Dr. Tabachnick scans the literature more widely he will find a number of cases in which the myasthenia appears to have been adversely affected by the hyperthyroidism.

FERGUS R. FERGUSON
L. A. LIVERSEDGE
E. C. HUTCHINSON.

Department of Neurology, Manchester Royal Infirmary.

7. McEachern, D., Ross, W. D. *Brain*, 1942, **65**, 181.
8. Hodges, R. J. H. *Lancet*, 1953, **i**, 143.
9. Churchill-Davidson, H. C. *Proc. R. Soc. Med.* 1955, **48**, 621.

## OCCUPATIONAL TREATMENT OF CHRONIC PSYCHOTICS

SIR,—In their admirable article (Nov. 12) Dr. Carstairs and his colleagues quote Galen as having written in A.D. 172: "Employment is nature's best physician, and is essential to human happiness." Would the authors add to my debt to them by giving the actual source where this wise saying can be found ?

London, S.W.1. SELWYN SELWYN-CLARKE.

## A REPORT FROM HOSPITAL

SIR,—Hospital administration by laymen has been much in the news. May I therefore report a recent incident ?

As an industrial doctor, I was asked if I could advise the management of the organisation in which I work about a patient in hospital. I accordingly wrote to the surgeon in whose ward he was and, at the same time, wrote to the patient asking for his permission for the report to be given. The surgeon promptly and very courteously replied and asked me to write for an official report to a gentleman who appeared to be the administrative chief of the hospital. This I did and again wrote to the patient to ask for his permission for the report to be made. In due course I received a letter from the house-surgeon giving me a useful report about the patient. The letter, however, was not sent to me direct but was forwarded under cover of a letter from the administrator.

Not to be outdone in what I now take to be the correct etiquette on these occasions, I wrote to thank the house-surgeon but sent the letter to the administrator with the request that he would pass it on.

London, N.1. R. E. W. FISHER.

## NEW SHORT-ACTING THIO-BARBITURATE

SIR,—Nobes[1] reported a series of 11 cases anæsthetised with sodium 5-allyl-5-iso-butylthiobarbiturate, now known as thialbutone sodium. I have used 'Transithal' brand of thialbutone sodium in over 100 cases, and this drug appears to have a definite place in anæsthetic and surgical practice.

It has proved extremely useful for external version, providing ample time and relaxation; and the unpremedicated mother can go home within 2 hours. It is equally useful for orthopædic manipulations, reduction of fractures, &c., the only reservation being that in the elderly less resilient patient lethargy may persist for 12–24 hours. It is also useful for short procedures such as dressings, cystoscopies, removal of retained products, and diagnostic dilatation and curettage.

Success largely depends on the induction, which is by intravenous injection, and it is of prime importance that this should be completed before anything is done which is likely to rouse the patient. The maximum dose for an adult is 1 g. in a 10% solution (10 ml.) given over a period of $4^1/_2$–5 minutes. The first part of the injection (between 1 ml. and 4 ml.) is given rapidly over a few seconds, and after a pause of $1^1/_2$ minutes the rest is given over the next $3$–$3^1/_2$ minutes. The size of the first injection depends on the age and condition of the patient and whether or not he is in the habit of taking alcohol or sedatives—e.g., aspirin, phenobarbitone, or "sleeping tablets." The young robust patient, the alcoholic, and the drug-taker all need a large initial dose, whereas the old, the frail, and the abstemious require a small one. The rate of the subsequent injection is dictated by the patient's reaction to the drug. With the correct rate of injection the patient may yawn once or twice and drop quietly off to sleep, if not stimulated or disturbed; but if the operation begins too soon or the patient is kept awake by chatter, it may be impossible to get him deep enough without adding another drug. If the injection is given too quickly the patient will sneeze, cough, or retch.

Thialbutone can be supplemented by another barbiturate or an inhalation anæsthetic. Once it was given for an examination under anæsthesia which proceeded to cæsarean section, and supplemented with nitrous oxide and suxamethonium bromide ('Brevidil M') it gave an excellent result comparable in every way to the sequence of hexobarbitone,

1. Nobes, P. *Lancet*, 1955, **i**, 797.

nitrous oxide, and suxamethonium bromide which I use as a routine for cæsarean section. When followed by nitrous-oxide/oxygen anæsthesia to supplement its effects, recovery is not delayed, and there are all the advantages of an intravenous induction with the rapid recovery of nitrous oxide. It does not appear to have any advantage over the established barbiturates for induction for major surgery.

With the help of Dr. Gordon Chorley, Dr. A. E. Nesling, and Staff-nurse J. A. Littlejohn of this hospital, blood-pressure readings and pulse-rates were recorded every minute during induction and maintenance of these cases. The records show that there is a slight transient fall in systolic pressure, little change in diastolic, and a slight slowing of the pulse during induction. The blood-pressure returned to normal 4–5 minutes after the start of the injection, and the pulse-rate within 2 minutes. The fall in blood-pressure is slight and has never called for measures to combat it. Once the blood-pressure starts to rise it appears that the patient is ready for operation.

A slight transient slowing of respirations and reduction in depth has also been noted; but there were no signs calling for the administration of oxygen in over 100 patients, whose ages varied from 17 to over 70.

There is considerable individual variation in the reaction to the drug, and it seems that the amount of the initial injection related to the patient's physique and habits is the important factor in judging this.

These remarks apply to the unpremedicated patient or the patient who has had nothing but atropine. In patients who have been premedicated with 'Omnopon' and scopolamine, or atropine and morphine, hypotension and bradycardia may be more striking and long-lasting; and, although recovery of consciousness may not be delayed, a period of lethargy and mild hypotension may ensue for 12 hours or more.

There has been no vomiting in patients who have not been prepared and have had a meal that day, and patients who have retched during induction have not been sick, although 2 patients who were "prepared" vomited slightly on coming round (they had had an opiate).

The important things to remember are: (i) the initial dose must be given quickly; (ii) it should be adjusted to the patient's condition and habits; (iii) the remainder should be given slowly, pause being made to allow any coughing, sneezing, or retching to settle, and the injection continued more slowly; (iv) no operations should begin until the whole dose has been given and the patient is sleeping quietly. If these precautions are disregarded there is a danger of a useful drug getting into disrepute before it has had a proper trial.

Messrs. May & Baker supplied the 'Transithal.'

Gloucester Royal Hospital. J. SHEGOG RUDDELL.

## ENURESIS

SIR,—Dr. Mark Bonnin, in his letter of Nov. 12, seems to have failed to appreciate that in your leader [1] it was correctly stated that the "conditioning" approach to the treatment of nocturnal enuresis originated by Mowrer [2] is used widely in the U.S.A.

Since our paper [3] appeared there have been very many requests and inquiries for the apparatus made and sold by the occupational-therapy department of the Colony for Epileptics, where it is produced at a tenth of the price mentioned by Dr. Bonnin.

It is difficult to devise a suitable, durable, and comfortable pad on which the patient may sleep. Even using nickel wire there is fairly rapid corrosion, and we are now experimenting with conducting rubber.

In Crosby's [4] original apparatus the arousal stimulus was a faradic shock, and rather complicated electrodes were fitted to the patient. We have found the bell perfectly satisfactory, and it obviates the use of genital electrodes and the "shock," both of which I feel are psychologically bad.

Some time ago a follow-up of 70 cases treated by this method showed that 75% were cured; and in many of these it proved effective when all other forms of treatment had failed.

The Orphan Homes of Scotland, Bridge of Weir, Renfrewshire. J. ROMANES DAVIDSON Medical Superintendent.

1. *Lancet*, 1955, i, 391.
2. Mowrer, O. H., Mowrer, W. M. *Amer. J. Orthopsychiat.* 1938, 8, 436.
3. Davidson, J. R., Douglass, E. *Brit. med. J.* 1950, i, 1345.
4. Crosby, N. D. *Med. J. Aust.* 1950, ii, 533.

## THE FORGOTTEN PATIENT

SIR,—In replying to an article written by a medical man about his own specialty I may show lack of discretion. But as one of thousands of laymen who give much of their time to helping to care for the mentally afflicted, I view this kind of article with alarm and resentment, because I know the damage they can do. I am sure that they are usually written with the best of intentions, but that does not make them any the less mischievous and misleading to the would-be nurse, to the relatives of patients, and to the general public, when they consist of half-truths or paint a picture in lurid colours.

I am not qualified to rebut Dr. Bickford's statement that "psychiatrists have failed to cure and discharge their patients," which seems to presume that they could cure but do not. But I do know the concern and distress it could cause in the mind of a person having a relative in a mental hospital, and the kind of reaction that might arise. Further, if we are to accept this contention, then we public representatives ought to be asking ourselves why public money is being spent on public servants who are not doing their job to the best of their ability.

Whatever may be Dr. Bickford's experiences in his own hospital, or elsewhere, he is grossly overstating some of the facts so far as the South West Metropolitan Region is concerned—a region that has far more mental-health beds than any other hospital region. Take, for instance, his claim that "in many hospitals droves of patients labour in the fields and cow-houses." A recent return in our region showed that, in the 24 mental hospitals and mental-deficiency hospitals that had farms attached or adjacent to them, 418 patients were engaged on farm work of one kind or another, and 265 patients were engaged in hospital gardens—a total of 683. The number of patients in those 24 hospitals at the time of the return was 31,173. A ratio of 1 : 119·4 engaged on farm work as such. "Droves" hardly seems the right word.

*The Old Folk.*—I am in full sympathy with Dr. Bickford's desire to serve the interest of old people who could be removed from a mental hospital if there were some other accommodation they could go to, and we have given the problem a great deal of attention and made it a point in our evidence to the Royal Commission on the Law relating to Mental Health. But in his anxiety to make a convincing case he is creating the impression that many old people who are not mentally ill are forced into mental hospitals, merely because there is nowhere else for them to go.

During our examination of the problem in our region we found that the 17 mental hospitals concerned had a total of 9887 patients over 65 years of age. Of these 971 were fit for other *hospital* accommodation, and 2348 were suitable for local-authority welfare accommodation But of the 3303 admissions of patients over 65 years of age in 1953, only 455 were suitable for other hospital accommodation and 105 for welfare institutions, and even some of those were borderline cases. In other words the great majority were rightly *admitted* to a mental hospital because they needed that form of treatment, but have so far recovered after treatment that they could leave now if there were other accommodation for them.

I know this is not a matter to be complacent about, but it is mischievous and wrong to suggest that most elderly people are forced into mental hospitals wrongly. Moreover Dr. Bickford did not mention that there are a number of old people in other accommodation who should be receiving psychiatric treatment and nursing.

*Absence of Incentive to Discharge Patients.*—As to the general charge that "doctors have little incentive to discharge their patients"—to which the obvious retort could be that the care and cure of their patients is their primary responsibility—it requires but little imagination to see the effect of this on patients or relatives who are being advised by their doctor to seek mental-hospital treatment. There is enough ignorance, prejudice, and misunderstanding already about the care and treatment of the mentally afflicted without statements of this kind being made to lend further colour to them—particularly at a time when great strides are being made in the direction of creating confidence in, and acceptance of, earlier diagnosis and treatment of mental instability.

Again I must talk about what we are doing in the South West Metropolitan Region, even at the risk of being thought boastful. Since April, 1953, we have reserved parts of several of our mental hospitals for the admission of non-statutory patients—i.e., patients without even the requirement of signing a "voluntary" order, who can walk out of the hospital at a moment's notice if they desire. Up to Sept. 30—two and a half years—3680 patients had been admitted to these beds, and a large proportion of these had been discharged as sufficiently recovered as not to require further hospital treatment. The average length of stay of these patients has been approximately six to eight weeks. The original number of such beds provided was 330, but since Oct. 1 it has been increased to 688, and it will steadily rise as more accommodation becomes available.

The more such facts are known and emphasised, the greater the confidence in psychiatric diagnosis and treatment; and, if this leads to greater coöperation between hospital, patient, and relative, the greater will be our service to suffering humanity.

*The Committee.*—My only comment about the kind of committee members described by Dr. Bickford is that either he must be grossly exaggerating or else he has an extraordinary preponderance of stupid and gullible people serving on the committees of which he has experience. Whatever other faults they may have, failure to visit every part of their hospital regularly and frequently, and to become very vocal about matters they think need remedying, cannot be laid at the door of the majority of members of hospital management committees that my mental-health committee control.

R. SARGOOD
Chairman, Mental Health Committee,
South West Metropolitan Regional
Hospital Board.

## MUSCLE IMBALANCE IN SCOLIOSIS

SIR,—In the article by Mr. Riddle and Mr. Roaf (June 18) there are certain features which should not go unchallenged. First, there is the conclusion that, apparently because "the spinal muscles were significantly stronger on the convex side at the apex of the curve," the cause of the curve was this over-activity. The authors do not mention the possibility that the over-activity is a result rather than a cause.

There seems to be confusion, too, in differentiating between inherent "strength" and the amount of activity at rest or during specific movements. These are *not* synonymous, though under certain controlled conditions they can be correlated. The suggested treatment—i.e., to "excise alternate laminæ and transverse processes at the apex of the curve on the convex side"—must therefore be highly questionable. It would be very interesting to know if the surgeons who referred patients have taken the advice of the authors in this regard. Another serious omission appears to be the absence of fibrillation potentials of denervation on the so-called weaker side. Surely it is pertinent to note the presence or the absence of this one sure electromyographic sign of denervation.

Finally, we must conclude from the significant conflict of data with needle and surface electrodes that this study requires greater expansion before any of the conclusions can be considered valid. Of course it has been long held that an imbalance of muscle activity, especially of rotators, is the probable underlying cause of scoliosis. However, the evidence presented in the article could be manipulated by the skilful antagonist of this theory, if such there be, to refute this belief rather than support it.

Department of Anatomy,
University of Toronto. J. V. BASMAJIAN.

## THE RING AND THE SWOLLEN FINGER

SIR,—Many methods have been used to remove rings from swollen fingers. For lesser degrees of swelling a little soap may suffice, or a thread wound round the distal part of the finger. With gross swelling such methods may fail and the patient may plead that the ring be cut off. At times a painful struggle may follow, ending with some damage to the finger if suitable instruments are not available. A description of a simpler technique for the removal of rings from grossly swollen fingers and its application in two cases may be of interest.

CASE 1.—A housewife, aged 28, had fractures of the left forearm. The displacement was corrected, plaster-of-paris applied, and her wedding ring removed. She was seen on the following evening when she was wearing the ring on the 4th finger of the right hand. She stated that even under normal conditions there was difficulty in putting the ring on this finger, which was now grossly swollen, congested, and painful. The usual methods having been tried without success, a solution of 2000 units of hyaluronidase in 1 ml. of water was injected subcutaneously into the proximal portion of the swollen area and under the ring, on the dorsum and sides of the finger, which was massaged gently to spread the injected solution. A thin rubber tube was then wrapped round the finger, commencing at the tip and continuing proximally up the finger, up to and including the ring. This was left in situ for 5 minutes. When it was removed the swelling had been dispersed sufficiently to permit the withdrawal of the ring without difficulty.

CASE 2.—A van driver, aged 51, had been struck on the dorsum of the left hand with a starting-handle. There was bruising over the 3rd and 4th metacarpophalangeal joints and 4th proximal interphalangeal joint. The 4th finger bore a heavy signet ring and was grossly swollen distal to this. A procedure similar to that used in the first case was carried out and the ring removed with ease.

An important contra-indication to this method would be evidence of sepsis in the affected digit, when there would be a danger of spreading the infection.

I have not seen this method recorded elsewhere, so I should like to draw attention to it because it may avoid injury to the patient and the ring.

I should like to thank Mr. H. W. C. Bailie, F.R.C.S., for permission to publish these cases.

Coleraine Hospital,
Northern Ireland. R. J. W. RYDER.

## TUBERCULOSIS OF THE PUBIS

SIR,—Bevan [1] has lately pointed out that the pubic bone is an uncommon site for tuberculosis and that cold-abscess formation from such a lesion seems peculiarly rare. In view of this apparent rarity I would like briefly to describe a further 4 cases which have occurred in this hospital since 1948.

A woman of 50, with a tuberculous left hip and dorsal spine, had a sinus in the left labia. Subsequent X-ray examination showed destruction and irregularity of the symphysis pubis. She was sent to a sanatorium where rest and chemotherapy resulted in healing of the sinus.

A woman of 31 presented with a painless spherical mass about $1\frac{1}{2}$ in. in diameter attached to the posterior aspect of the left upper border of the symphysis pubis. X-ray examination showed widening and partial destruction with some new bone formation of the symphysis pubis. There was

1. Bevan, P. G. *Brit. med. J.* Oct. 1, 1955, p. 832.

also an associated metastatic osteolytic lesion with a sinus of the proximal phalanx of the left hallux. Her condition did not improve with conservative measures, including streptomycin and isoniazid, and she was finally transferred to a sanatorium where the pubic cold abscess was curetted and the cavity packed with bone chips. Subsequent X-ray films showed solid fusion across the symphysis.

A woman of 65 presented with a painful inflammatory swelling over the inner and upper aspect of the left thigh in the adductor region, which was incised and drained. Subsequent X-ray examination of the pelvis showed an osteolytic lesion of the symphysis pubis and left ascending ramus with irregularity and destruction of bone. Culture of the pus showed tubercle bacilli. A small sinus persisted for many months but finally healed, without any further operative treatment, on chemotherapy.

A man of 22, a physical-training instructor, complained of pain in the region of the right adductor tubercle. This condition was regarded as a probable traumatic periostitis, but X-ray examination during the next twelve to eighteen months showed there was an infective osteitis of the pubis with a possible pulmonary lesion. His symptoms eventually subsided after a prolonged period of rest and a course of streptomycin and *p*-aminosalicylic acid.

Hackney Hospital,
London, E.9. R. F. READ.

## ARGENTAFFIN CARCINOMA

SIR,—The observation by Dr. Snow and his colleagues (Nov. 12) that some patients with metastasising carcinoid tumours are extremely sensitive to alcohol is of great interest to those engaged in the prevention of alcoholism. Chance observations, such as these and others (e.g., alcohol-induced pain in Hodgkin's disease [1]), may help us eventually to find a means of readjusting physiological imbalance as a cause of alcoholism. The advent of disulfiram ('Antabuse') has stimulated interest in substances or ailments causing "aversion" to alcohol, which include: hydrogen sulphide, tetraethyl lead,[2] Hodgkin's disease, cyanamide, the edible mushroom *Coprinus atramentarius*, animal charcoal, and pyrazolone derivatives. An article discussing the "anti-alcoholic" properties of all these is appearing on p. 98 of the *International Journal on Alcohol and Alcoholism*, 1955.

Isleworth, Middlesex. H. PULLAR-STRECKER.

SIR,—Dr. Stacey suggests, in his letter last week, that a thrombocytopenia might explain certain anomalous biochemical changes reported by Dr. Goble, Dr. Hay, and myself (Nov. 12). We found, however, that platelet-counts remained within normal limits throughout the remission induced by $^{198}Au$, and at no time was there any clinical evidence of thrombocytopenia.

In our view, even if thrombocytopenia had occurred it could not possibly account for our findings, for the following reasons:

5-hydroxyindoleacetic acid (5-H.I.A.A.) levels indicated that daily release of 5-hydroxytryptamine (5-H.T.) into the circulation by the tumour mass remained approximately constant. Since platelets absorb free 5-H.T. from the surrounding plasma, had their production been diminished a temporary rise in free plasma-5-H.T. level would have occurred. Although this might have been reduced to pre-thrombocytopenic levels by the mono-amine oxidase mechanism, giving rise to a decreased *total* serum-5-H.T. level, there would have been no reduction in free plasma-5-H.T. and consequently no reduction in urinary 5-H.T. excretion. And since the weight of pharmacological and clinical evidence suggests that 5-H.T. is the humoral agent responsible for many of the clinical findings in the argentaffin-carcinoma syndrome, neither would there have been any remission of symptoms, for it is difficult to see how a reduction in platelet-bound 5-H.T. alone could give rise to this.

Consequently we considered that some enhancement of the mono-amine oxidase mechanism, possibly by temporary inactivation of an inhibitor, might explain the puzzling biochemical findings accompanying the clinical remission; these findings consisted in a constant urinary excretion of 5-H.I.A.A. despite decreased serum and urinary 5-H.T. levels, and not decreased 5-H.T. levels alone as stated by Dr. Stacey.

Department of Pathology,
Royal Free Hospital,
London, W.C.1. M. SANDLER.

1. Bichel, J., Bastrup-Madsen, P. *Lancet*, 1953, i, 764.
2. Walker, G., Boyd, P. R. *Ibid*, 1952, ii, 467.

## UNRESTRICTED VISITING IN A CHILDREN'S WARD

SIR,—We read the article by Dr. Campbell and her colleagues (Nov. 5) with envy and admiration—envy because they have had eight years of unrestricted visiting as opposed to our two years of a similar kind of experiment. We have been admitting mothers of children of the fretful age into our cubicles, where we have just room for an adult bed beside the cot. The mother is by her infant or child day and night. There are no amenities specially designed for mothers. Their meals are brought to them by nurses or orderlies as if for a patient. They are not, at first, asked to do anything but stay with their child. They are not prisoners in their cubicles but they seldom, in fact, want to be away for more than a brief rest.

These mothers see the whole treatment of their child and take part in it as far as possible, helping in many small useful ways. They also see some of what goes on in the ward as a whole. If we were to try to illustrate here some of the great benefits all round that have resulted, we would find ourselves reiterating all the points so excellently put in the article from Queen Victoria Hospital, Melbourne.

There are, of course, things which apply specially to the smaller children. When treatment is complex or disturbing, nursing may sometimes be more difficult owing to the clinging attitude of the child to the mother. We have not yet had enough experience to make any generalisations about this except to say that we think it does not matter; whereas when the child has to endure these things alone and cannot cling to anyone, harm may be done.

By publishing articles and letters from time to time on this subject, you, Sir, are doing a lot to break the still-frozen attitude of many of our hospitals towards nursing by the mother, free visiting, or even daily visiting, and to parents in general.

The work of the nursing staffs of hospitals in the care of sick children has been a magnificent achievement, and it is well known that this covers not only bodily care but mental comfort to the utmost that the unnatural conditions of a children's ward will allow. But it has too long been a tradition to present to visiting parents the picture of an orderly ward with children wanting for nothing as far as outward attention goes, and to spare them the pain of seeing what children sometimes have to endure in the form of medical or surgical treatment. To work in the constant presence of the parents has long been regarded as impracticable, but it is not, as Dr. Campbell and her colleagues have shown, and we also have found. The first step in getting over the old prejudice, and towards the whole-hearted acceptance of parents in the child's illness, is to realise that in our treatment of sick children we have nothing to hide. We may fear our work being misunderstood by onlookers, but that possibility is something that can be dealt with.

Children's Department,
Amersham General Hospital,
Bucks. DERMOD MACCARTHY
MARY LINDSAY
I. MORRIS.

SIR,—I was very interested to read the article by Dr. Campbell and her colleagues. The Children's Department of Pembury Hospital has also allowed unrestricted visiting for the past six years, and as in the Australian experiment we have found it an unqualified success. Our experience has been so similar to that described in the article that no comment on it is required.

I should like simply to add one point. To the medical and nursing staff, contemplating the introduction of unrestricted visiting, it might appear that the wards will for ever be infested with hordes of visitors. In actual fact it turns out quite differently, and instead of the periodic invasion at set visiting-times there are always a few visitors, who do not interfere with the running of the ward at all.

Children's Department,
Pembury Hospital, Kent. N. M. JACOBY.

### IMMUNOHÆMATOLOGY

SIR,—In your leading article of Nov. 5 you say:

"An example is the drug sensitivity caused by 'Sedormid' or quinidine; these drugs probably modify platelets, thus producing iso-antibodies; later auto-antibodies develop, by a process of which we know nothing, and these antibodies act only in the presence of the sensitising drug . . ."

Could some of the evidence be given showing that two sorts of antibody are developed in patients sensitised with these drugs?

Department of Chemical Pathology,
Westminster Medical School,
London, S.W.1. DAVID MARRACK.

*** In the leader we were drawing mainly on the findings of M. Stefanini and of J. F. Ackroyd, whose articles we cited. To our regret we did not make this clear at all points.—ED. L.

### BACKACHE AND POLIOMYELITIS

SIR,—It is surprising that so little stress is laid on the symptom of backache in the diagnosis of anterior poliomyelitis in its pre-paralytic phase.

If it were more widely recognised that pre-paralytic poliomyelitis sometimes manifests itself by backache and mild pyrexia, and that complete rest in bed in this pre-paralytic phase lessens the chance of severe paralysis, many fatalities from this disease might be avoided.

Among the hundreds of cases of "pyrexia of unknown origin" that were admitted to hospital in North Africa in the late war, it became possible to diagnose both poliomyelitis and variola because of this symptom, before the full clinical picture showed itself. In my experience considerable backache is uncommon in other feverish illnesses.

Bedford. J. H. EASTON.

### PHENYLBUTAZONE FOR HERPES ZOSTER

SIR,—In the treatment of herpes zoster no remedy has proved fully satisfactory. I have tested the value of phenylbutazone, with promising results.

A woman, aged 60, who had had thoracic herpes, suffered severe postherpetic neuralgia which was unrelieved by various different measures. 3 ml. of a 20% solution of phenylbutazone was injected intramuscularly, and within twenty-four hours the pain was much reduced. After a second injection the patient, who previously had been unable to sleep because of pain, was able to sleep. After the fourth injection the pain ceased completely, and it has not recurred.

In view of this dramatic success further cases were treated in this way. In the first 11 cases there has been no failure; and it has proved unnecessary to give more than four or five injections of phenylbutazone. Oral administration of the drug has not proved satisfactory.

These results suggest that phenylbutazone should be administered at the start of the illness.

Nicosia, Cyprus. GEORGE PARTELIDES.

### C. E. RHODES

SIR,—The medical profession will have noted with pride the posthumous award of the Albert Medal to the late Surgeon Lieutenant Charles Eric Rhodes, R.N.V.R., as recorded in your columns a fortnight ago.

Eric Rhodes was an enthusiastic member and sometime secretary of the United Hospitals Sailing Club, and the club has started an appeal for funds to help his wife and daughter. A plaque recording his heroism is to be placed in the clubhouse at Burnham-on-Crouch.

Many of your readers may wish to contribute to this appeal. Donations should be sent to me at University College Hospital Medical School, London, W.C.1.

M. L. ROSENHEIM
Hon. Treasurer, United Hospitals Sailing Club.

### CHRISTMAS GIFTS FUND

SIR,—I would like to remind your readers who have not yet responded to the President's appeal (Oct. 8, p. 773) that it is our custom to distribute the gifts some days before Christmas. I hope that all who can will send their contributions, marked "Christmas Gifts," to the Secretary, Royal Medical Benevolent Fund, 1, Balliol House, Manor Fields, Putney, London, S.W.15, as soon as possible.

F. A. JULER
Hon. treasurer.

## Public Health

### Smog in the North-West

SOMETHING like the notorious London smog of December, 1952, covered Manchester, Salford, and surrounding areas on Thursday, Nov. 17, and less densely on Nov. 18. The fog seemed to be rather less thick than the London smog; it was dirty grey, without the yellowish tinge of the London variety. We are indebted to Dr. J. L. Burn, medical officer of health for Salford, for the following details.

In Salford the concentration of smoke was heavy on Thursday morning and late afternoon, an average of 2·67 mg. per cubic metre being recorded. The following table shows that the sulphur-oxide concentration several times exceeded the highest level recorded in the London smog (1·34 parts per million).

| *Time* (*Nov. 17*) | *Smoke* (*mg. per c.m.*) | *Sulphur oxides* (*p.p.m.*) |
|---|---|---|
| 10.00–11.00 A.M. | 3·06 | 0·730 |
| 11.00–12.00 NOON | 2·20 | 1·376 |
| 12.00– 1.00 P.M. | 1·89 | 1·469 |
| 1.00– 2.00 P.M. | 1·89 | 1·469 |
| 2.00– 3.00 P.M. | 2·02 | 1·551 |
| 3.00– 4.00 P.M. | 2·20 | 1·376 |
| 4.00– 5.00 P.M. | 4·67 | 1·582 |
| Average | 2·67 | 1·347 |

The average smoke concentration in Salford for November, 1954, when conditions were by no means ideal (though free from obvious smog), was 0·63 mg., sulphur oxides 0·188 p.p.m. On Friday, Nov. 18, the corresponding figures were:

| *Time* (*Nov 18*) | *Smoke* (*mg. per c.m.*) | *Sulphur oxides* (*p.p.m.*) |
|---|---|---|
| 10.00–11.00 A.M. | 3·16 | 1·582 |
| 11.00–12.00 NOON | 3·46 | 0·619 |
| 12.00– 1.00 P.M. | 5·16 | 1·205 |
| 1.00– 2.00 P.M. | 3·06 | 0·609 |
| 2.00– 3.00 P.M. | 2·53 | 0·712 |
| 3.00– 4.00 P.M. | 1·95 | 0·730 |
| 4.00– 5.00 P.M. | 2·30 | 0·615 |
| Average | 3·09 | 0·867 |

It can be seen that the smoke pollution increased slightly on Friday and the concentration of sulphur oxides decreased appreciably. Saturday, Nov. 19, was generally misty, and only clear in patches in the area. It was noticeable that on Thursday and Friday the fog was not so uniformly dense as in the great London smog; indeed there were patches in the area of the Manchester conurbation where it was comparatively clear. It was also clear on Saturday, and Sunday again showed improvement. During the forty-eight hours ended at 11.30 A.M. on Monday, Nov. 21, the concentration of smoke was 1·06 mg. per c.m. and sulphur oxides 0·415 p.p.m. The inversion phenomenon characteristic of the London smog was noted. There was a layer of cold air up to 800 feet; anticyclonic conditions prevailed and there was little or no movement of the smog during the first two days.

The full effects of the smog on health may not be apparent for some time, but it was at once clear that it caused distress to people who had to go about their business. It certainly merited something more than the description given in the report[1] on the London smog—

1. Mortality and Morbidity during the London fog of December, 1952. Report by a committee of departmental officers and expert advisers appointed by the Minister of Health.

"little more than a nuisance" to healthy persons. Local hospitals have reported a slight increase in the admission-rate for respiratory and cardiovascular disease. The suddenness of the onset of the smog was doubtless responsible for the fact that few smog masks were seen; but a brisk demand for them was reported on the second day.

As part of the investigation into the effects of the fog in Salford, Dr. Burn is writing to local doctors to ask them about their experiences.

### Poliomyelitis

The seasonal fall in the notifications of poliomyelitis continues. Total uncorrected notifications in England and Wales for the week ending Nov. 12 (45th week) were (44th week in parentheses): paralytic 127 (154), non-paralytic 99 (105), total 226 (259). The proportion of non-paralytic cases is still higher than usual though it has declined in recent weeks.

At a meeting of the American Public Health Association in Kansas City last week, a team of experts declared that the Salk vaccine was now safe.[1] It was reported that no suggestion of danger had been found in any batch of vaccine made by any manufacturer since the safety rules were revised on May 13. The new rules had not weakened the vaccine; one dose seemed to be as effective now as three were last year. Preliminary results from 11 States showed an attack-rate 2–5 times greater in unvaccinated children.

### Fluoridation of Water-supplies

Before authorising the four demonstrations of the fluoridation of water-supplies which are being arranged in England and Wales, the Minister of Health made a close study of the research which had been carried out in America, and he satisfied himself that there was every justification for the demonstrations. He thought it right to give the Standing Medical Advisory Committee an opportunity of putting their own views on record, and has now been advised by the committee that: "Despite many years of observation and investigation there is no scientific or medical evidence at present available suggesting that there is any risk in drinking water containing added fluoride in the concentration of one part per million."

A public meeting at Watford on Nov. 19 passed a resolution opposing a scheme to introduce fluoride into the town's drinking-water as an experiment in the prevention of dental decay.[2] In the discussion, the arguments against fluoridation were given as "nervous and medical damage, destruction of confidence in the public health services, councillors making medical decisions for others, a community at loggerheads, and denial of the right to decide what one takes into one's body."

### Statistics of Incapacity

The Ministry of Pensions and National Insurance has gathered statistics about sickness and injury among the working population. Most of these figures do not justify general publication, but requests for information received from time to time from medical research-workers, medical officers of health, and others suggest that it would be useful to distribute the figures to those likely to be interested. The first collection of statistics (for 1950) was sent two years ago to medical officers of health of counties, county boroughs, and (in Scotland) large burghs and to individuals of whose interest the Ministry had become aware. Its reception warranted the preparation of a further digest of statistics for 1951–52; and a new collection, relating mainly to 1953–54 is just ready.

The statistics are based on medical certificates sent to the Ministry with claims to benefit. They do not include illnesses of two or three days for which no claims are made, or sickness in certain persons not eligible to claim. Thus, as a measure of the incapacitating sickness among the working population, they are incomplete. The introduction to the digest is designed to aid intelligent interpretation of the tables and to prevent misleading conclusions being drawn from them.

1. *Times*, Nov. 16, 1955.
2. *Ibid*, Nov. 21, 1955.

## Parliament

### Bill to Abolish the Death Penalty

IN the House of Commons on Nov. 15, Mr. SYDNEY SILVERMAN was given leave under the ten-minute rule to introduce a Bill to abolish, or for a period suspend, the passing and execution of the death sentence on conviction of murder and to substitute an alternative penalty. For the past 25 years the House, he said, had had no substantial doubt as to the side which it supported in this matter. If effect had not been given to the desire to see this evil thing removed from the Statute Book it had been due only to the obstinate and relentless opposition of the Home Office. He did not know what dark, secret, noisome influence it was in the Home Office that seduced every Home Secretary in turn, but it was known from the announcements made last week[1] that every one of the major unanimous recommendations of the Royal Commission, for whose report the House had been asked to wait, had now been rejected by the Government. He did not think that the House really wished the matter to stand where the Home Secretary had left it without further discussion and examination. He knew that there was hardly a Member of the House who did not in his heart believe that this reform must come and must come quickly. The Bill was given a first reading.

### QUESTION TIME

#### Ban on Heroin to be Retained

Mr. H. M. KING asked the Minister of Health what reply he had given to recent protests of the medical profession made to him against the proposed banning of the manufacture of heroin.—Mr. IAIN MACLEOD: That I did not feel justified in departing from the advice I had given to the Home Secretary, after consulting the Standing Medical Advisory Committee.

#### Harmful Publications

Replying to a question, Major GWILYM LLOYD GEORGE, the Home Secretary, said that since the Children and Young Persons (Harmful Publications) Act came into force on June 6 only 1 complaint had reached him. He understood that 3 other works had been brought to the attention of the Director of Public Prosecutions and that in none of these cases did the Attorney-General consider that proceedings were called for.

#### Ban on Agene

Replying to a question, Mr. HEATHCOAT AMORY, Minister of Agriculture, said that the arrangements made by the flour-millers and flour-importers provided for nitrogen trichloride in any form to cease to be used in flour by the end of this year.

#### Extraction-rate of Bread

Dr. BARNETT STROSS asked the Minister whether he was aware that flour used in baking standard national bread was at times of a higher extraction-rate than is laid down by regulations; and what steps were being taken to ensure that the regulation was complied with.—Mr. AMORY: I am aware that, because of certain technical difficulties which have arisen in the practical application of the provisions of the Flour Order, the present situation is unsatisfactory. This was one of the considerations which led the Government in May to appoint a panel to make an independent assessment of the composition and nutritional value of flour of varying extraction-rates.

#### Amalgamation of Forces' Medical Services

Replying to a question whether, in order to save medical man-power and public money, he would consider amalgamating the medical services in the three Fighting Services and forming one defence medical service, Mr. SELWYN LLOYD said that the amalgamation of the medical services of the Armed Forces was rejected by the Government of the day early in 1948. It was one of the matters which had been examined by the committee under Lord Waverley on the medical and dental services of the Forces. Their report was now being considered. In due course the Government's decision on this would be announced.

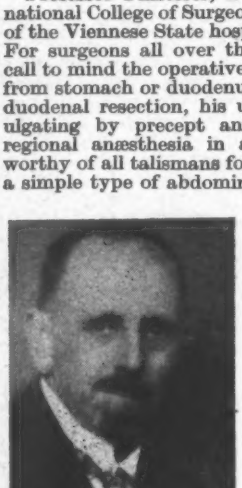
1. See *Lancet*, Nov. 19, 1955, p. 1086.

# Obituary

## HANS FINSTERER

M.D. Vienna

Professor Finsterer, a former president of the International College of Surgeons and a former surgeon-in-chief of the Viennese State hospitals, died in Vienna on Nov. 4. For surgeons all over the world his name will at once call to mind the operative treatment of ulcer hæmorrhage from stomach or duodenum, special techniques in gastroduodenal resection, his unabating enthusiasm in promulgating by precept and practice the advantages of regional anæsthesia in abdominal surgery, and (least worthy of all talismans for securing surgical immortality) a simple type of abdominal retractor.



He was born in 1877 at Weng in Upper Austria, where his father was a farmer. In 1902, after graduating in medicine at the University of Vienna, he became an assistant to Hochenegg at the second surgical clinic of the Allgemeines Krankenhaus. Apart from an interlude of three years which he spent working under Hacker at Graz, he remained with Hochenegg, and in 1913 he was appointed to a lectureship in surgery at the university.

During the 1914–18 war he worked in a garrison hospital in Vienna. In 1920 he was appointed professor extraordinarius. For the next fifteen years or so he worked only in private hospitals, and he used to bemoan his limited facilities for preoperative investigation. Perhaps because he was not attached to any of the great teaching centres, he gave much of his time to postgraduate education. This interest enabled many foreigners to study his technique, and T. H. S. recalls how in the 'twenties and 'thirties it was the fashion of many young, and not so young, surgeons to visit Vienna to see Hans Finsterer at work.

"His handling of gastric lesions was something from which everybody could learn, and he was above all a great exponent of local anæsthetic technique in the performance of gastrectomy. Visitors to his small hospital or private clinics were usually allowed to assist, and one wonders how great is the debt of gratitude owed to him for his teachings in this type of work. His results from early operation in cases of severe hæmatemesis were incomparably better than any other method could show at that time, and it was not only the excellent results that he obtained in gastrectomy but the impetus he gave towards surgical safety in the upper abdomen."

H. C. E., another of these surgical visitors, gives a lively picture of a morning spent with Finsterer.

"At whatever time one arrived to see him operate, one was always late, or so it seemed. Billed to start at, say, 7.30 A.M., he would already have his first case under way before that time, so that at one's first attendance, when one was still not fully conscious, one saw a pair of hands belonging to a short, round-shouldered figure, with kindly eyes peering through spectacles above a mask. The hands were clothed in white cotton gloves superimposed over rubber gloves. The cotton gloves were used to swab, and were repeatedly changed throughout the operation. Few words were spoken by him as he worked. Despite the handicap of two pairs of gloves covering the stumpy fingers, the precision of movement was masterly. Though the operation often took a long time—one in which he removed an immense growth of the colon previously turned down as inoperable by another surgeon took 5½ hours—one's interest never flagged. He was not a slow operator. The time he took was due to his meticulous technique and to the fact that his extirpation of cancer was radical.

"His operations were always performed under regional and splanchnic block, the effect of which would wear off after two hours or so. The patient would then complain in no uncertain terms, and a nurse carrying an ether bottle would appear to subdue him. The patient having been quietened, the nurse would disappear, and the patient would regain consciousness with the operation still in progress. If necessary, the ether experience would then be repeated.

"The operation completed, and the operation mask removed, one saw a kindly bearded face. Finsterer would then disappear to dress, and in a few minutes would reappear in the shabbiest suit imaginable. He would don a soiled raincoat and a dilapidated felt hat, and prepare to visit another hospital. On the first occasion I accompanied him, we boarded a tram—no chauffeur-driven limousine for Finsterer—and as we strap-hung, he produced a brown-paper pack from his raincoat pocket in which were two bread rolls, which he proceeded to eat then and there. This was his breakfast."

Between the two wars Vienna was no longer wealthy, and Finsterer worked under handicaps which might have deterred a lesser man. C. A. P. relates how he used instruments and equipment old and in disrepair, which obviously he was unable to replace.

"Yet he managed" (C. A. P. continues) "to have the essentials. The keynote of his work was this recognition of what is vital in human operations and what allows of individual variation. This was the secret of his brilliant results. He was an unassuming kindly man, an introvert rather than an extrovert, and he was forced into prominence by the sheer merit of his contributions to surgery. It is gratifying that his worth was recognised in 1935 by his appointment as surgeon-in-chief of all the official State hospitals of Vienna."

Essentially a man of peace, Finsterer was wholly absorbed in the problems of surgery and he was undisturbed by vicissitudes in the political environment of his land. Yet during the late war he suffered like other Austrians, and his friend G. G.-T. has a photograph taken during the Russian sweep through Austria in which "a sad and wan little Finsterer contrasts with the warrior Sergei Yudin standing beside him." To Finsterer as a surgeon G. G.-T. pays the following tribute:

"He will be remembered longest for his work in advocating and practising surgery in the treatment of ulcer-hæmorrhage, his demand for early operation if these cases were to be saved, his insistence on that 'fatal third day,' when the scales became heavily loaded against successful surgery, and above all his uncompromising insistence on the employment of regional and splanchnic anæsthesia for these most anxious cases.

"Like many Continental surgeons he made every effort to conserve the sphincter in operations for cancer of the rectum, perhaps thereby neglecting the pathological findings of the English school of proctology. One of his last papers dealt with the interpolation of a piece of small intestine to bridge the gap between the proximal colon and the ampulla of the rectum—an operation justified not only by the recovery-rate, but by the end-results.

"Throughout his whole career he was an intransigent advocate of regional anæsthesia in abdominal surgery, and candidates for laparotomy were refused admission to the surgical beds under his control unless they were willing to forgo general narcosis. The diminished mortality of gastrectomy performed under regional anæsthesia was sufficiently impressive to attract to his operating-theatre surgeons from every land, including surgical travelling clubs from Britain. He was no supreme surgical craftsman, he had no university chair, yet from his private clinics he delivered a message to the surgical world. His 'resection for exclusion' operation for unresectable duodenal ulcer remains an important contribution to surgical technique. He visited my own operating-theatre on several occasions, and he was always a welcome guest in England. His interest in surgical problems remained undimmed till the end. It was good to have known honest, trusty, friendly Hans Finsterer."

## ARCHIBALD DODD

M.D. Lpool, D.P.H.

Dr. Dodd, who retired earlier this year from his appointment as medical officer for the Fylde division of Lancashire, died at his home in Kirkham on Oct. 20. He went to school at St. Helens, where his father later became mayor, and continued his studies at Liverpool University, where he graduated M.B. with honours in 1927. After experience in hospital and as ship's surgeon, he spent some years in general practice in Manchester, and later in Liverpool. but he gave it up for health

reasons and entered the public-health service. He took the D.P.H. with distinction in 1937 and the M.D. a year later. He held appointments as assistant M.O.H. for Birkenhead and as deputy M.O.H. for Dewsbury before he entered the service of the Lancashire county council. During the late war, he served as a hygiene specialist and was granted the honorary rank of lieut.-colonel.

E. D. I. and J. W. P. write: "Archie Dodd was big of frame and generous of heart; we who knew him well from his early student days enjoyed his friendship and jovial company. He was sympathetic with the less fortunate and, as might be expected of one with such an open and gifted nature, he soon gained the confidence and affection of all with whom he was associated. Though ill health dogged him, he loved the country and country pursuits and found much that was congenial to him in his Lancashire appointment."

Dr. Dodd leaves a widow and a daughter.

## SETON SIDNEY PRINGLE

O.B.E., M.Ch. Dubl., F.R.C.S.I.

Mr. Seton Pringle, who died at his home at Kilmessan, co. Meath, on Nov. 10, during a distinguished career in Irish surgery had received the highest honours which his colleagues in Dublin could offer him.

Born in 1879, he was educated at Campbell College, Belfast, and at Trinity College, Dublin. He graduated B.A. in 1902, and took the M.B. the following year. As a student he gained the Fitzpatrick scholarship, and he was awarded the Hutchinson Stewart scholarship for distinguished answering in the final M.B. examination.

In 1905 he was elected F.R.C.S.I., and in the succeeding years he was appointed surgeon to Mercer's Hospital, Dublin, and the Cork Street Fever Hospital. He was also examiner in surgery for the Royal College of Surgeons in Ireland. During the first world war he was surgeon to the Red Cross Hospital, Dublin Castle, and from 1917 to 1919 he was officer commanding the Irish Counties War Hospital with the rank of lieut.-colonel. In 1918 he was appointed surgeon to the Royal City of Dublin Hospital, and he was consulting surgeon to many others, including the Rotunda Hospital, the Royal Hospital for Incurables, the Drumcondra Hospital, and the Royal Victoria Eye and Ear Hospital. In 1925 he was appointed honorary lecturer in the pathology of bone in Trinity College, Dublin, a personal appointment which was described as "for the present holder only." The University of Dublin conferred the degree of M.CH. on him in 1930, and six years later he was elected president of the Royal College of Surgeons in Ireland. In 1940 he was further honoured by the presidency of the Royal Academy of Medicine in Ireland—a body in which, with its many specialist sections, all the disciplines of medicine are fused.

He had always been a keen fisherman and a first-class shot, and when he retired from practice in 1944 he became an enthusiastic farmer. His first wife, Miss Ethel Munn of Ballymote, co. Sligo, died in 1938, and he later married Miss Eileen Blandford, who survives him and who is president of the council of the St. John Ambulance Brigade in Ireland.

## JAN PAUL STRÖMBECK

M.D.

Professor Strömbeck, of Stockholm, who died in August, had wide interests as a surgeon, and his many papers ranged over abdominal surgery, urology, and the surgery of bones, joints, and blood-vessels. Born in 1896, he qualified in 1924 and worked at the Serafimer Hospital in Stockholm from 1928 till in 1939 he was appointed professor of surgery at Lund. In 1949, on the retirement of Professor Söderlund, Strömbeck succeeded him at the Serafimer Hospital, at the same time becoming professor of surgery at the Karolinska Institute. In addition to his clinical studies, he did experimental work on animals, including investigation of tumours of the bladder; and his advice was often sought on ethical and other problems not directly connected with his professorial chair.

---

Captain A. N. CAHUSAC, O.B.E., M.C., who died on Nov. 14, was chief secretary of the St. John Ambulance Association from 1918 to 1953. He was chairman of many revision committees of the association's textbooks and editor of most of the new publications.

# Diary of the Week

NOV. 27 TO DEC. 3

### Monday, 28th

UNIVERSITY OF LONDON, Senate House, Malet Street, W.C.1
6 P.M. Prof. J. Nuttin (Louvain): Motivation and Cognitive Factors in Human Behaviour. (First of three lectures.)

UNIVERSITY COLLEGE, Gower Street, W.C.1
5.30 P.M. (Physiology theatre.) Dr. W. S. Feldberg, F.R.S.: Rôle of Mediators in the Inflammatory Tissue Response.

INSTITUTE OF OBSTETRICS AND GYNÆCOLOGY
4.30 P.M. (Chelsea Hospital for Women, S.W.3.) Mr. J. H. M. Beattie: Functional Uterine Hæmorrhage.

BIRMINGHAM MEDICAL INSTITUTE, 154, Great Charles Street, Birmingham, 3
8 P.M. *Anæsthetics.* Dr. J. A. Lee: Anæsthetic Outpatient Clinics.

MANCHESTER MEDICAL SOCIETY
5 P.M. (Medical School, University of Manchester.) *Odontology.* Dr. M. J. McArdle: Facial Neuralgia.
9 P.M. *General Practice.* Dr. C. E. B. Rickards: Outpatient Gynæcology.

### Tuesday, 29th

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, London, W.C.2
5 P.M. Dr. F. Dudley Hart: Hormone Replacement Therapy in the Surgery of Endocrine Disorder. (Arris and Gale lecture.)

BRITISH POSTGRADUATE MEDICAL FEDERATION
5.30 P.M. (London School of Hygiene and Tropical Medicine, Keppel Street, W.C.1.) Dr. G. S. Dawes: Physiological Effects of Anoxia in the Fœtal and Newborn Lamb.

INSTITUTE OF NEUROLOGY
5.30 P.M. (National Hospital, Queen Square, W.C.1.) Prof. C. A. Keele: Therapeutics of Pain.

INSTITUTE OF DERMATOLOGY, Lisle Street, W.C.2
5.30 P.M. Dr. F. R. Bettley: Eczema-asthma Syndrome.

ST. MARY'S HOSPITAL MEDICAL SCHOOL, Paddington, W.2
5 P.M. Prof. Andrew Claye: Disturbances of Sexual Function.

ROYAL STATISTICAL SOCIETY
5.30 P.M. (Westminster Medical School, Horseferry Road, S.W.1.) Dr. A. H. T. Robb-Smith: From Graunt to Geneva.

THE HOWARD LEAGUE FOR PENAL REFORM, Abbey Orchard Street, S.W.1
6.30 P.M. Dr. Peter Sainsbury: Social Aspects of Suicide in London. Dr. Erwin Stengel: Reactions of Society to Attempted Suicide.

### Wednesday, 30th

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1
8.30 P.M. Lord Radcliffe: How a Lawyer Thinks. (Lloyd Roberts lecture.)

POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road, W.12
2 P.M. Dr. Peter Bishop: Endocrinological Investigations.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330 Gray's Inn Road, W.C.1
5.30 P.M. Dr. I. Friedmann: Ulcerative Granulomatous Conditions of the Nose.

INSTITUTE OF ORTHOPÆDICS, 234, Great Portland Street, W.1
8 P.M. Mr. H. J. Burrows, Mr. W. H. Tuck: Orthopædics in the West Indies.

NOTTINGHAM MEDICO-CHIRURGICAL SOCIETY, 64, St. James's Street, Nottingham
8.30 P.M. Dr. F. S. Cooksey: Medical Rehabilitation.

ROYAL FACULTY OF PHYSICIANS AND SURGEONS, 242, St. Vincent Street, Glasgow, C.2
5 P.M. Dr. P. R. Peacock: Possible Ætiological Factors in Lung Cancer.

### Thursday, 1st

ROYAL COLLEGE OF SURGEONS OF ENGLAND
5.30 P.M. Dr. S. P. Meadows: Cranial Palsies and Otolaryngology.

BRITISH POSTGRADUATE MEDICAL FEDERATION
5.30 P.M. (London School of Hygiene and Tropical Medicine.) Dr. J. Walker: The Oxygen Environment of the Fœtus.

ROYAL SOCIETY OF MEDICINE
5 P.M. *United Services.* Colonel L. R. S. Macfarlane, Lieut.-Colonel R. L. Townsend, Captain T. M. Robinson: Immunisation against Tuberculosis in the Army.
8 P.M. *Neurology.* Dr. Henry Miller, Dr. William Blackwood: Neurological Complications of the Acute Specific Fevers. Dr. C. E. Lumsden: Experimental Allergic Encephalitis.

LIVERPOOL MEDICAL INSTITUTION, 114, Mount Pleasant, Liverpool, 3
8 P.M. Dr. C. H. Stewart-Hess, Dr. F. Hopkins: Anxiety States.

UNIVERSITY OF ST. ANDREWS, Queen's College, Small's Wynd, Dundee
5 P.M. Prof. G. F. Boddie, M.R.C.V.S.: Eradication of Bovine Tuberculosis.

### Friday, 2nd

UNIVERSITY OF LONDON
5 P.M. (Charing Cross Hospital Medical School, Chandos Place, W.C.2.) Dr. R. K. Burns (Washington): Experimental Studies of Sex Differentiation in the Opossum.

ROYAL SOCIETY OF MEDICINE
10.30 A.M. *Otology.* Miss Edith Whetnall, Mr. I. S. D. Thomson, Dr. D. C. Kendall: Management of Deafness in the Young Child.
2.30 P.M. *Laryngology.* Dr. Frank Elliott, Dr. John Harman, Mr. Charles Keogh: Pharyngeal Paralysis.
5.30 P.M. *Anæsthetics.* Dr. A. Bracken, Dr. R. Woolmer: Carbon-dioxide Accumulations in Anæsthetic Circuits.

POSTGRADUATE MEDICAL SCHOOL OF LONDON
2 P.M. Mr. Hedley Atkins: Research into Breast Cancer.
4 P.M. Dr. A. G. MacGregor: Radioactive-iodine Therapy.

INSTITUTE OF OBSTETRICS AND GYNÆCOLOGY
3 P.M. (Hammersmith Hospital, Ducane Road, W.12.) Mr. Stanley Way: Intraepithelial Carcinoma.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY
3.30 P.M. Dr. C. H. Edwards: Headaches and Neuralgias.

KETTLE LECTURE
5 P.M. (Royal Infirmary, Cardiff.) Prof. J. H. Dible: Ischæmia in the Peripheral Circulation.

# Notes and News

## JUBILEE OF THE UNIVERSITY OF MALAYA

ON Oct. 15 the first fifty years of higher education in Malaya were celebrated in Singapore. Mr. Malcolm Macdonald, chancellor of the university, presided at a graduation ceremony when 200 degrees were conferred, including 38 M.B.B.S. Prof. David Mekie, F.R.C.S.E., who is retiring from Malaya, was made the first professor emeritus of the university. The honorary degree of M.D. was conferred on Sir Philip Manson-Bahr, Dr. C. V. Jumeaux, and Dr. A. J. Thumboo. Lord Reading, a Minister of State for Foreign Affairs, was present at a dinner held in the evening, and afterwards a cup of Malayan silver was given to Mr. Macdonald for his work towards interracial harmony. Lady Manson-Bahr presented the prizes for university athletics.

Scientific meetings held in connection with the celebrations included a lecture on the discovery of tropical medicine and its impact on the world, by Sir Philip Manson-Bahr, and a symposium on tuberculosis and the changing concepts of dentistry. At an entertainment organised by the students and given in the Oei Tiong Ham Hall, the chief feature was a modernised version of Molière's *Médeçin malgré lui*.

Dr. D. W. G. Faris, dean of the university, was chairman of the golden jubilee committee.

## SPENDING BY HOSPITALS

THE Minister of Health, in a letter to the chairmen of hospital authorities, asks for their coöperation in the Government's measures to meet the national economic situation. He remarks that it is not intended to reduce allocations or the expanded hospital building programme, but asks that spending be kept within the total sums allocated and that work proceeded with as part of the expanded building programme shall be essential work of undoubted urgency.

## MEDICAL RESEARCH IN AUCKLAND

Our NEW ZEALAND CORRESPONDENT writes: The Auckland division of the British Empire Cancer Campaign recently appealed for £50,000 to buy a super-voltage therapy unit for Auckland Hospital, and collected £130,000. The balance is largely to be used for research, and a project involving the search for chemical substances having a bearing on cancer, particularly as possible agents in treatment, is planned. The organic chemistry department of Auckland University College, which has had experience of this work in relation to native flora under Prof. L. H. Briggs, is to carry out the task. Also planned are extensions of tissue-culture and other techniques to do with screening these and other compounds, under Dr. J. F. Burton, of the pathology department of Auckland Hospital.

The Auckland Medical Research Foundation has recently been launched by Mr. John Grierson, chairman of the Auckland Hospital Board. At present the collection of money is its chief object.

## FOOD AND AGRICULTURE

THE Food and Agricultural Organisation of the United Nations has just celebrated its tenth anniversary, and its annual report [1] reviews the dramatic transformation in some aspects of agriculture during this decade. There has been much progress in the development of technological and physical resources. World consumption of commercial fertilisers is at almost twice the pre-war level, and the world tractor population has increased threefold. Advances in plant breeding, in the control of plant diseases and pests, and in animal husbandry have led to greatly increased food production in certain parts of the world. A beginning has been made with a vast programme for better control and use of water.

Unfortunately the geographical distribution of these developments is most uneven. In Asia agricultural production is barely keeping pace with population increases. The average calorie intake for Ceylon, India, Japan, Pakistan, and the Philippines is only just over 1800 per head per day. The corresponding figure for Australia and New Zealand is 3200 and for Canada and the U.S.A. 3100. In these countries agricultural production is far outstripping both home consumption and the usual export trade. The U.S.A., Canada, and Australia had 42·3 million metric tons of wheat in stock before this year's harvest was brought in. This is three times as much as in 1951. Such a stock represents about two years' exports. The U.S.A. could probably meet all normal demands for home consumption and export even if the farmers sowed no wheat for the 1956 harvest. There are also substantial surpluses of coarse grains, tobacco, cotton, and sugar in America. These huge surpluses have not led to a catastrophic fall in prices because most of them are held by governments which are committed to a policy of keeping up farm prices. The disposal of these stocks is a formidable problem, and a threat to the stability of national economies. The report does not suggest any economic means for orderly transfer of this surplus to needy countries. It does point out the desirability of industrialisation in underdeveloped countries. A small industrial population limits the market for sales off farms; and a high rural-population density restricts the size of farms and so limits agricultural efficiency. Surplus supplies in highly developed countries might be used to help finance more rapid economic development in underdeveloped countries.

This valuable report shows clearly that agriculture in America is approaching a crisis, in which we may all be implicated.

1. The State of Food and Agriculture, 1955. H.M. Stationery Office. Pp. 235. 12s. 6d.

## FOR THY STOMACH'S SAKE

SHERRY has been drunk in England at least since the 14th century, and, as Mr. Rupert Croft-Cooke makes clear in his unabashedly partial history of the wine,[1] for most of the time with enthusiasm. But like other tried favourites it has had temporary setbacks. In the 19th century, for instance, sherry was the victim of a whispering campaign inspired, Mr. Croft-Cooke suggests, by teetotalers, envious importers of French and German wines, and the powerful brewers. Malicious rumours were circulated that sherry was "plastered" and "fortified" by the addition of large quantities of gypsum and proof alcohol, which made it injurious to health and conducive to gout. Among its champions sherry numbered John Ruskin and George Augustus Sala, but even their powerful pens were unable to silence these calumnies. Inquiries about sherry became such a nuisance to the medical profession that in 1898 *The Lancet* decided to send an analytical commission to Jerez. According to Mr. Croft-Cooke the visit is still remembered. "The Lancet Commission," he relates, "were given freedom to go where they liked and took full advantage of it. 'My father told me,' said one bodeguero to me this summer, 'that he never knew when one of them would pop out from behind a barrel.'" As a result of these conscientious inquiries the commissioners produced an exhaustive report which exonerated sherry from any charge of adulteration, and all talk of plastering and fortifying was dropped. Since the 'thirties sherry has been enjoying another period of great popularity; and in his chapter on "when and how" to drink it Mr. Croft-Cooke claims that there can be few times of the day or night when a glass of sherry is unwelcome, save perhaps to that awkward person the man "who has just had his tea." But even he will enjoy this book.

1. Sherry. By RUPERT CROFT-COOKE. London: Putnam. 1955. Pp. 232. 21s.

## A FILM FOR EXPECTANT MOTHERS

MORE antenatal clinics are using films to instruct their patients in the anatomy and physiology of childbirth, and many show a film of a delivery to selected expectant mothers. A new film designed to tell primigravida about the antenatal clinic and the course of labour has been made for the National Birthday Trust Fund by Dr. W. A. Bullen, Mrs. Blazeby, and Miss Jean Burton-Brown, F.R.C.S. *My First Baby* (16 mm., sound, black-and-white, 25 min.) tells in "flash-back" the story of a young mother from the time she first visits her doctor after missing two periods. At her early visits to the antenatal clinic she hears about diet, the importance of regular urine, blood-pressure, and weight checks, and the rhesus blood test. The significance of the examination for piles, varicose veins, and a tightening wedding ring is also suggested. The anatomy of birth is shown in an animated sequence; and there are references to exercises and relaxation classes and the care of the breasts (a breast-milk apparatus is demonstrated with reference to the milk-bank). After a description of the analgesics commonly used during labour, the last ten minutes of the film gives a detailed account of the patient's labour.

This excellent film successfully approaches childbirth from the patient's viewpoint. The commentary by the mother is beautifully delivered, and the pictures are lively and closely related to the commentary. The film compares very favourably with the French *Painless Childbirth*[1] designed for the same purpose for use in a French antenatal clinic.

*My First Baby* may be obtained on hire or purchase from Boleyn Films, 37, High Street, Sandwich, Kent.

## INDEX OF PHARMACEUTICAL PREPARATIONS

THE Index of New Products issued by the *Pharmaceutical Journal* now covers about a thousand preparations. Each new preparation is dealt with on a card which states in conveniently readable form its composition, properties, indications, packing and price, and suppliers, and also references to published reports. Included in this service is a therapeutic index, or index of cross-references, which is issued half-yearly as a booklet and together with an index of analagous preparations makes it easier to pick a way through the growing collection of cards. Subscriptions (two guineas per annum) should be sent to the *Pharmaceutical Journal*, 33, Bedford Place, London, W.C.1.

## DOCTOR AT LARGE

THE prescription is *Rep. mist.* Those who enjoyed *Doctor in the House* and *Doctor at Sea* will also be tickled by this account[2] of a newly qualified doctor in search of a job. Chestnuts? Yes, but they are *marrons glacés*.

## CARDS IN GOOD CAUSES

CHRISTMAS cards serve two good purposes, instead of one, if they are bought from the charitable bodies that nowadays raise funds by their sale. Besides the cards, various decorative accessories are also to be had, which likewise exemplify two aspects of the Christmas spirit.

This year we have not seen many new cards; but the National Association for Mental Health have issued three—a reproduction of a Florentine figure of the Madonna and Child, a modern nativity design by Anthony Lewis, and a picture of a child praying by a French artist of the 15th century. The charming study by Augustus John, the picture of the boy with his donkey from the film *Never Take "No" for an Answer*, and the reproduction of the statuette of the dimple-cheeked Virgin with the Laughing Child are again available. These cards cost 6*s*. 6*d*. a dozen, including envelopes, and may be obtained from 39, Queen Anne Street, London, W.1.

"Holiday bound—the world around" is the theme of the five new cards designed by Eddy Legrand for the United Nations Children's Fund (UNICEF) which hopes to sell a million cards in Great Britain this year for the welfare of needy children throughout the world. The cards are in bright colours and show children of different nationalities at play; the season's greetings are printed in five languages. In addition there is a card with the symbol of the United Nations surrounded by the flags of the member nations in colour, designed by Antonio Frasconi, and cards which have been popular in previous years, including "The Torch of Hope" by Henri Matisse. All cards cost 7*s*. 6*d*. for 10, including envelopes, and can be had from 14–15, Stratford Place, W.1.

The double-barred red cross of the National Association for the Prevention of Tuberculosis (Tavistock House North, Tavistock Square, W.C.1) is now a familiar symbol, and the association is anxious to sell 110 million Christmas seals this year to help its good work. The seals cost 4*s*. for a block of 100, and Christmas cards with similar designs are 5*s*. a dozen with envelopes.

The Grenfell Association, of 66, Victoria Street, S.W.1, which is doing such valuable medical work in Labrador and Northern Newfoundland, hopes that a successful Christmas-card season will help to provide its mission in Newfoundland with a much-needed ambulance. An illustrated leaflet describing the cards, which are colourful and "Christmassy," costs 1½*d*.

The National Spastics Society has opened three new schools for spastic children this year and is selling gaily coloured seals at 1*d*. each in sheets of 12. Its address is 28, Fitzroy Square, W.1.

"Fougasse's" inimitable style and economy of line give character to the cards and Christmas stationery of the Universities Federation for Animal Welfare (UFAW), 7a, Lamb's Conduit Passage, W.C.1. His latest card is in colour and depicts a circle of varied and (we should have thought) incompatible animals linking paws and hooves and singing "Auld Lang Syne." A mixed packet of 6 cards is sold with envelopes for 3*s*. Fougasse also illustrated Rosalind Hill's amusing little book *Both Small and Great Beasts* (2*s*. 6*d*. post free), and his own anthology about animals called *The Neighbours* (8*s*.).

1. See *Lancet*, 1955, 1, 1231.
2. Richard Gordon. London: Michael Joseph. 1955. Pp. 208. 10*s*. 6*d*.

## University of Cambridge

On Nov. 12 the following degrees were conferred:

*M.B., B.Chir.*—Barbara V. Leney (by proxy).
*M.B.*—F. B. Mann.

The Raymond Horton-Smith Prize for 1954–55 has been awarded to Dr. E. M. M. Besterman (Trinity College) for his thesis on the value of phonocardiography in rheumatic carditis.

## University of London

Dr. Charles Harris has been appointed deputy vice-chancellor for the remainder of the year 1955–56.

Mr. E. O'F. Walsh, PH.D., senior lecturer in the department of physiology at the Royal Free Hospital School of Medicine, has been appointed to the university readership in biochemistry at that school.

The following have passed the final examination for the degree of M.B., B.S.:

*Honours.*—M. R. H. Ashken (*b*), Middlesex; J. R. T. Colley (*c*), St. Thomas's; J. E. Cullis (*c*), St. Thomas's; Doreen A. Lowman (*c*), Charing Cross; Ruth Pinder (*c*, *d*, *university medal*), Roy. Free; Pamela M. Sherman (*c*), St. Thomas's.

(*b*) distinguished in medicine; (*c*) distinguished in applied pharmacology and therapeutics; (*d*) distinguished in surgery; (*e*) distinguished in obstetrics and gynæcology.

*Pass.*—John Aaron, J. B. Akingba, C. O. Alele, J. H. R. Allen, Anne Ambrose, Flora J. Anderson, J. T. Andrews, G. P. Anthony, J. R. Anthony, T. I. F. Arthur, R. P. Ashfield, E. J. Ashworth, D. W. Atherley, J. O. Atunrase, F. A. Awobodu, J. R. Axon, Joan W. Baker, M. J. Ball, E. E. P. Barnard, Margaret A. Barrie, P. A. Bartlett, B. W. Barton, Moira A. Batchelor, A. E. Bennett, E. P. C. Benson, Edith Bergel, A. T. Birmingham, D. H. Black, Sheila Blake, J. W. Blaxland, Audrey M. Bloom, G. R. Bonner-Morgan, Jean-Marie R. Boucherat, Robert Jean M. Boucherat, R. D. Bradley, D. E. Brooke, R. B. Brown, N. D. F. Browne, E. M. Buchan, A. A. Buchanan, P. S. C. Bunning, Anne J. Burge, I. A. Campbell, P. F. R. Cantin, I. R. Cardy, B. P. Carroll, Enid J. Cartwright, Audrey L. Carus, T. B. Catnach, Devendranathan Chanmugam, A. R. L. Clark, J. M. Clark, Jean E. Clark, B. S. Clarke, J. J. Clarke, G. M. Clayton, Benjamin Cobb, Lester Cohen, Barbara B. Collier, Bernard J. E. Cooke, J. A. Cox, John Crarer, Iain Crawford, Peter Crossley Meates, D. R. Crouch, Peter Curzen, S. L. Dale, J. O. Dalrymple, J. R. Daly, Rosemary L. Dart, Eileen M. Darwood, Jean M. Davidson, J. M. P. Davies, T. G. G. Davies, T. G. Davies, Ann Davis, Caroline J. H. Davson, Gesualda de Gabriele, Oliver de Sola Pinto, A. R. Dewsbury, W. R. O. Eggington, P. D. Elder, C. d'A. Ellis, G. H. Ellis, P. M. Elwin, I. R. H. Evans, Muriel E. Evans, R. G. B. Evans, R. F. Everton, Ekpo Edet Eyo, Christine M. Fairclough, J. G. Fairer, D. R. Farmer, Judith F. Farrar, C. A. Fawole, L. J. Fish, G. S. Flack, P. C. Fleming, A. P. Fletcher, J. M. Forster, J. G. Francis, A. C. Fraser, M. J. Freeth, Truls Frøtchen, Shirley M. Frow, D. W. Gabriel, N. St. C. Gainer, Elizabeth P. Gibbs, A. G. Giddins, P. J. Giffard, D. C. Gill, N. W. Glendinning, G. C. Gould, John Goulton, Jacqueline A. Gowers, C. W. Graham-Stewart, J. A. Greeves, J. D. Grice, Joan M. Gunn, H. M. R. Hacker, J. S. Hall, Thomas Hargreaves, D. T. Harrison, G. R. Hart, Constance E. Haughton, G. C. B. Hawes, M. J. Healy, B. H. P. Heber, I. N. Henderson, Jon Henderson, R. I. Henry, Sylvia K. Hepton, Anita M. Herdan, K. T. Hesketh, A. D. Hickman, J. C. Hill, P. N. A. Holden, D. H. G. Hopkins, K. E. Howells, Christine T. T. Hughes, J. W. G. Hughes, John Hunnybun, Warwick Hutchings, D. C. Hutfield, B. B. Hyman, A. C. Ikeme, M. H. K. Irwin, Millar Oboada Adafe Ja Ja, D. C. James, W. D. Jeans, D. R. John, Janet R. C. Jones, J. S. P. Jones, T. G. Jones, Y. D. Jones, W. H. Jones, J. V. Keefe, D. J. Kelsall, J. O. P. Kerley, P. N. Kersley, G. E. King, H. A. P. King, Imogen E. King, R. A. Lacey, John Landon, B. K. Lane, I. N. Lee, A. F. Lever, Yuin Betty Ling, Dawn C. M. Llewellyn, J. K. Lloyd, Evelyn C. Lock, B. A. Lovell, A. H. Luscombe, Alfred Lytton, J. C. McAlpine, J. L. McClure, I. S. MacDougall, A. I. H. MacFarlane, H. R. T. A. McLeod, Mary Maguire, D. M. Mann, J. E. L. Mann, Dulcie A. L. Manning, Alexander Marrack, A. J. Martin, C. M. Montegriffo, M. R. Morton, Robert Nall, Ignace J. M. Y. Nalletamby, J. D. Nelms, Margaret E. Noad, P. O. Nwachukwu, Jean S. M. Ogden, E. D. A. Oremond, W. D. H. Parry, B. J. Penry, Margot C. Pepper, I. S. T. Philpotts, Theresa E. E. Piper, J. K. Powell, Patricia M. Powell, H. F. Price, Raymond Radford, J. A. Reynolds, D. M. D. Rice, A. G. Rickenbach, Joan Ridley, G. R. E. Roberts, R. W. K. Rogers, J. H. Ronaldson, R. P. Rosswick, Jean Rotherham, Barrymore Schiff, G. W. Scott, Philip Sharer, D. J. Sills, I. S. G. Sim, R. T. Sims, I. D. Smith, E. O. G. Sofekun, Catherine I. Soutter, J. A. Stainton-Ellis, M. B. Stanton, Rosemary E. Stephenson, J. B. Stillwell, H. M. Swallow, Elizabeth A. Symes, J. H. K. Taylor, J. J. Taylor, K. E. Thomas, R. J. Thomas, J. W. Thomson, G. D. Tompkins, J. S. Toner, M. G. P. Venn, Shirin Abdulhussein Visram, P. F. Wale, A. R. Walker, C. J. Wallace, Jean M. Watkins, R. C. Watson, H. A. Williams, I. S. Wilson, T. M. Winstanley, Mary E. Wood, P. H. N. Wood, Marian L. Woodford, N. D. Woodrow, J. A. Wright, Peter Wright, Janet C. J. Young.

### University of Sheffield

Dr. D. A. Heath has been appointed honorary demonstrator in pathology.

### Royal College of Physicians and Surgeons of Canada

At the convocation of the annual meeting of the college, held in Quebec on Oct. 22, the honorary fellowship was conferred on Sir Harry Platt, president of the Royal College of Surgeons of England.

### International Congress of Gastro-enterology

The fifth meeting of the Association des Sociétés Européennes et Méditerranéennes de Gastro-Entérologie will be held in London next year from July 18 to 21 under the presidency of Dr. Thomas Hunt. The subjects chosen for discussion are: ulcerative colitis, premalignant conditions of the gastro-intestinal tract, and non-malignant diseases of the œsophagus. Further particulars may be had from the hon. secretary, Mr. Hermon Taylor, London Hospital, E.1.

### International Congress of Clinical Chemistry

This congress, which is sponsored by the International Federation of Clinical Chemistry and the Commission of Clinical Chemistry of the International Union of Pure and Applied Chemistry, is to be held in New York City from Sept. 9 to 14, 1956. Further information may be had from the congress secretary, Mr. John C. Reinhold, PH.D., 711, Maloney Building, Hospital of the University of Pennsylvania, Philadelphia 4, Pa., U.S.A.

### Nutrition Society

On Monday, Dec. 5, at 5 P.M., at 1, Wimpole Street, London, W.1, a meeting of this society will be held when Dr. H. J. Deuel, jun., professor of biochemistry and nutrition in the University of Southern California, will speak on fat as an essential component of diet.

### Drummond Fellowships

Applications are invited for a Drummond senior fellowship (£900 p.a.) and 2 Drummond junior fellowships (£500 p.a.) for research in nutrition. The fellowships will normally be tenable for two years. Application forms must be returned to the hon. secretary, Drummond Trust, University College London, Gower Street, W.C.1, not later than Jan. 27.

### British Association of Urological Surgeons Home and Overseas

Next year the annual meeting of this association will be held in Liverpool on Thursday, Friday, and Saturday, June 28, 29, and 30. The programme will include a discussion on the use of the intestine in urology, when Prof. Charles Wells will be the opening speaker. Further particulars can be had from Mr. J. Cosbie Ross, 72, Rodney Street, Liverpool, 1.

### Institute of Child Health, London

The Simpson Smith prize for 1955 (100 guineas) has been awarded to Mr. H. H. Nixon for his essay on intestinal obstruction in the neonatal period.

Dr. J. E. Hall has been appointed lecturer in physiology, Dr. J. M. Tanner lecturer in child health at the child-study centre, and Dr. A. D. M. Jackson, assistant to the Nuffield professor of child health.

### Sheffield United Hospitals

A radiotherapy centre with 60 beds is to be built with a legacy of £100,000 left during the late war by Alderman J. G. Graves to the old court of management of the Royal Sheffield Infirmary and Hospital. The hospitals' endowment fund will also supplement the Treasury allocation of £65,000 for 1956–57 so that the proposed schemes for a new psychiatric department and a children's outpatient department may both go forward.

### Mental Health Conference

On Thursday, Jan. 26, at B.M.A. House, London, W.C.1, the Central Council for Health Education is to hold a conference to consider the rôle of local authorities in promoting mental health through health education. Dr. A. Dalzell Ward will speak on training personnel in preventive mental-health work. Further particulars may be had from the secretary of the council, Tavistock House North, Tavistock Square, W.C.1.

### Symposium on Vitamin $B_{12}$

The first European symposium on this vitamin is to be held in Hamburg from May 22 to 26, 1956, under the presidency of Prof. J. Kühnau and Prof. A. Jores. Those who wish to take part should write to Dr. H. C. Heinrich, Physiologisch-chemisches Institut, 52, Martinistrasse, Hamburg, 20.

### London Amateur Boxing Association

A meeting of the medical officers of this association will be held on Monday, Dec. 5, at 8 P.M., at the Great Northern Hotel, Kings Cross. Dr. Edwin Clarke will speak on head injuries.

### Society of Medical Officers of Health

*Services group.*—The annual dinner of this group will be held on Friday, Dec. 9, at the R.A.M.C. headquarters mess at Millbank, London, S.W.1, at 7.30 P.M. Tickets (£1 1*s.*) may be had from the administrative officer of the society, Tavistock House South, Tavistock Square, W.C.1.

### Rockefeller Grants

During the third quarter of this year the Rockefeller Foundation have allocated $1,076,000 in grants. These include:

$34,100, to be available during the next four years, to the department of preventive and social medicine, directed by Dr. LeRoy Allen, at the Christian Medical College, Vellore, India.

$13,000 to St. Mary's Hospital Medical School, London, for equipment for research on protein metabolism and enzymology under the direction of Dr. Albert Neuberger, F.R.S.

## Appointments

BURNS, T. H. S., M.A., B.M. Oxfd, F.F.A. R.C.S., D.A.: anæsthetist, St. Thomas's Hospital, London.

COLQUITT, H. R., M.D. Lond., M.R.C.P.: whole-time consultant pathologist, Barnsley and Rotherham areas.

FOWLER, J. M., M.B. Glasg.: appointed factory doctor, Denny, Stirlingshire.

GLASS, D. T., M.D. Belf., D.M.R.D.: consultant radiologist, Mid-Ulster Hospital, Magherafelt, co. Londonderry.

* HOWELL-JONES, H., F.F.A. R.C.S., D.A.: hon. anæsthetist, Hôpital et Dispensaire Français, London.

MCFARLAND, W.D.H., M.B. Belf., D.P.H.: M.O.H., Stafford.

MCLAREN, MARGARET E., M.B. Glasg., D.P.H.: deputy M.O.H. and School M.O., Smethwick.

MARSHALL, BERNARD, M.B. St. And. D.O.M.S.: part-time consultant, ophthalmologist, Sheffield.

MERIVALE, W. H. H., M.B. Lond., M.R.C.P.: director of the department of clinical pathology and consultant clinical pathologist, Guy's Hospital, London.

MILLCHAP, GORDON, M.D. Lond.: visiting scientist, clinical centre, National Institute of Neurological Diseases and Blindness, Bethesda, Maryland, U.S.A.

RICHARDSON, J. E., M.S. Lond., F.R.C.S.: part-time consultant in general surgery, London Hospital.

STONE, D. G. H., M.B. Lond., M.R.C.P., D.C.H.: part-time consultant paediatrician, N. Lincolnshire.

THOMPSON, J. A., M.B. Belf.: appointed factory doctor, Dulais Valley, Glamorgan.

**South-Western Regional Hospital Board:**

MERRYWEATHER, REGINALD, M.B. Lond., F.R.C.S.: consultant orthopædic surgeon, N. Gloucestershire clinical area.

THOMSON, J. L. G., M.D. Lond., D.M.R.D.: consultant radiologist, Bristol clinical area.

YOUINGS, M. D., M.B. Lond.: S.H.M.O. in infectious diseases, Plymouth clinical area.

**East Anglian Regional Hospital Board:**

GALVIN, C., M.CH., F.R.C.S.: senior surgical registrar, United Norwich hospitals.

GARDEZI, S. A. R., M.B. Punjab.: surgical registrar, Peterborough Memorial Hospital.

MAHMOOD, M. R. H., M.B. Punjab.: Ipswich and East Suffolk Hospital (Anglesea Road wing).

MARTIN, J. A. M., M.B. Lond., D.L.O.: registrar in E.N.T. surgery Norfolk and Norwich Hospital and Jenny Lind Hospital.

**Colonial Appointments:**

ABAYOMI-COLE, A. B., M.B. Durh.: senior M.O., Sierra Leone.

BOARDMAN, H. M. S., L.R.C.P.E.: A.D.M.S., Sierra Leone.

BRADBURY, E., B.CHIR. Camb.: D.D.M.S., Sierra Leone.

COOKE, E. R. N., M.D. Dubl.: specialist (pathologist), Kenya.

CUMMINGS, G. G., M.B., D.T.M., D.P.H.: D.D.M. and H.S., Hong-Kong.

DEAN, N. M. B., M.B. Edin., F.R.C.S.: senior specialist, eastern region, Nigeria.

EVANS, W. J. M., M.B. Lond.: D.D.M.S., Tanganyika.

LIGHTBOURNE, HYACINTH I., M.B. Birm: senior M.O., Jamaica.

PHILLIPS, P. M. J., M.R.C.S.: principal M.O., Gold Coast.

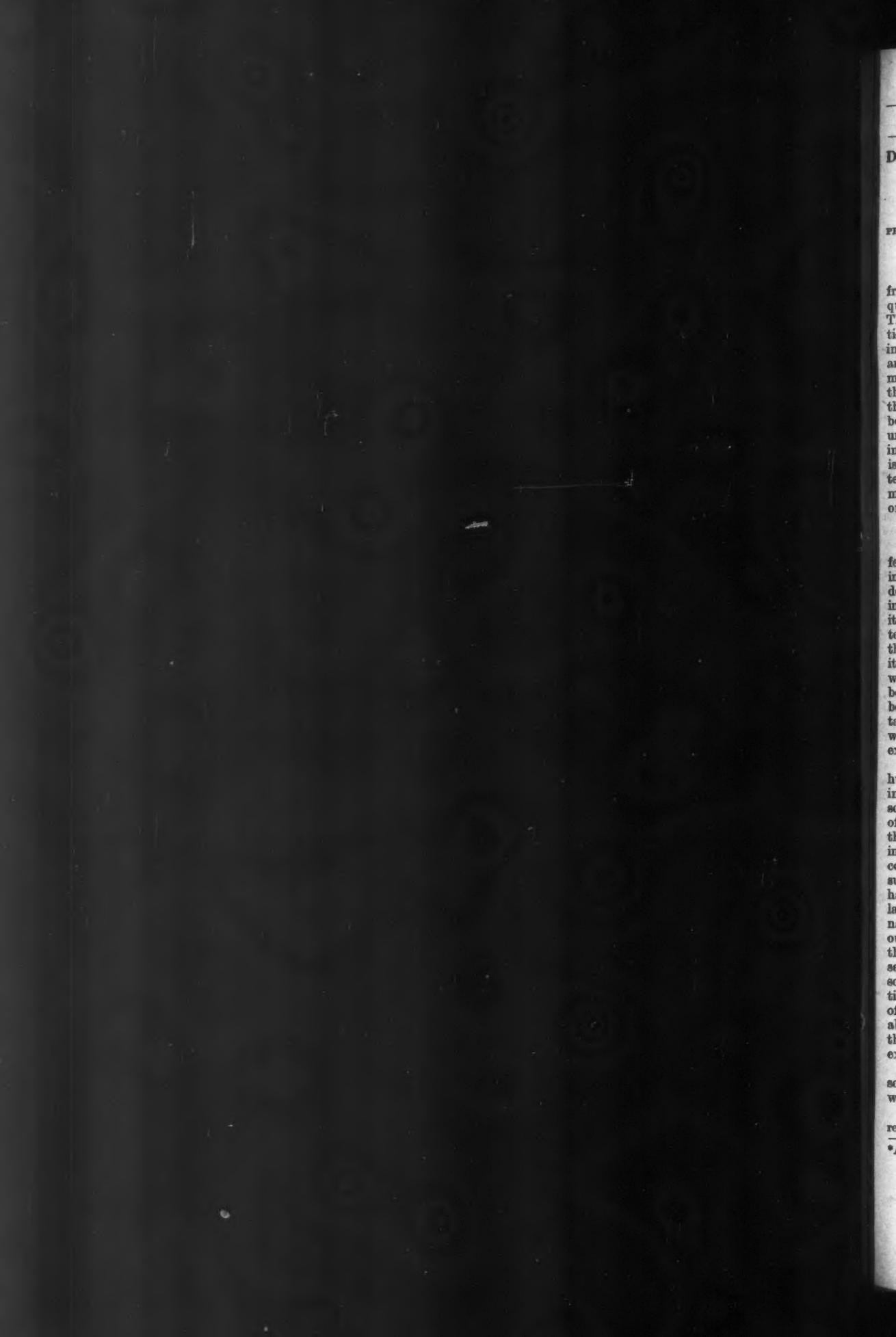
RIGBY, E. P., M.B. Lond.: A.D.M.S., Kenya.

ROSS, A. D., M.B. Edin.: sleeping sickness M.O., northern region, Nigeria.

SCOTT, DAVID, M.B. Camb.: specialist, epidemiologist, Gold Coast.

STRISIVER, E. V., M.D. Berlin, F.R.C.S.: senior specialist (surgical), Sierra Leone.

* Amended notice.



# DISORDERS OF CONTEMPORARY SOCIETY* AND THEIR IMPACT ON MEDICINE

G. W. PICKERING
M.A., M.D. Camb., F.R.C.P., F.A.C.P. (Hon.)
PROFESSOR OF MEDICINE, UNIVERSITY OF LONDON; DIRECTOR OF THE MEDICAL UNIT, ST. MARY'S HOSPITAL, LONDON

MANY of the worst ills of organisation and outlook from which we suffer today in medicine are due to two quite different processes occurring in society as a whole. The first is the growth of strongly centralised administration, and of associations, trade unions, or parties which impose strict rules on their members. These result in an important, and to my mind serious, disease which may perhaps be named compulsory uniformity. I regard this as a serious disease partly because I cannot think that it can be to the ultimate good of mankind, and because it expresses extremely powerful forces which we understand dimly, or not at all, and which we have no immediate prospect of controlling. The second process is a very different one. It is the growth of science and technology. This has produced a series of relatively minor disorders, many of which we could remedy, if only more of us realised the need.

## Compulsory Uniformity

An urge to conform to the behaviour of the rest of our fellow creatures is one of the strongest motivating forces in human affairs. This urge was first clearly defined and described by my old teacher Wilfred Trotter. The herd instinct, as he called it, is the basis of human society; it is the cement which binds together the family, the team, the firm, the institution, the political party, and the nation. It is the basis of education by precept; since it is fortunately the urge of the young to imitate those who, for the time being, they regard as their masters or betters. The herd instinct is thus a part of human behaviour that we have to accept because it is an elementary property of man. It is also a property without which civilised society, as we now know it, could not exist or persist.

In every country at every time and in every branch of human endeavour, there has also existed an urge to improve on Nature and to force others to conform to some code of behaviour. This again is an essential part of civilised society, finding its expression in the law of the land, and in the regulations without which no institution could for long conduct itself. The reason why countries like the United States and Great Britain are such satisfactory places in which to live is because we have evolved a very reasonable system of law, and this law is enforced. (If only some reasonable code of international law could be drawn up and enforced, many of our troubles would be at an end.) Having mentioned the word reasonable, I would like to stress it, because it seems to me that the essence of a lively and interesting society is the absence of unnecessary rules and restrictions. Too many rules and regulations carry the penalties of producing a very stereotyped form of existence, and of abolishing initiative. Life, in fact, becomes dull; and that, I think, is tragic because life should be such an exciting adventure.

To give an example of this generalised disorder of society, let me quote from a speech of Mr. Narayan, who was the heir to the leadership of Mr. Nehru in India.

"There is a tendency to forget the human being. We remember groups, classes, religions. We think of the workers; the capitalists, the Asians, the Americans, the Russians; but we forget the individual men. . . . Humiliating Western domination has shaken the Asians' faith in their traditional ways. They have come to associate their plight exclusively with the lack of material power, and they are turning their energies ever more insistently to the achievement of such power. But in their efforts they tend to forget the human being, to overgovern, to legislate even on matters of individual conscience. And they have come, in the short year of their freedom, to accept that everything should be done through legislation."[1]

## STANDARDISED TRAINING

I first became aware of what I regard as a pathological desire to make all doctors alike some three or four years after the end of the war, when two proposals were under discussion in Great Britain. The first was a proposal in one large university to abolish one of the alternative routes which students have been able to follow for the early part of the medical curriculum. In Great Britain, boys and girls enter universities from school at the age of 18 or 19, having spent from one to four years in the vith form in which they may receive specialist education to quite a high level. In England candidates who have done enough general science and who prove it by passing the requisite examination are excused the course in general science at the university. The proposal was to abolish this exemption and to treat boys who had done a lot of science and those who had done little exactly alike. The second was a series of proposals to lay down in detail the posts which men should hold over a period of four years before they could be eligible to hold consultant posts in the various specialties in the National Health Service.

A small calculation will show the effects of the two proposals. In Great Britain the medical curriculum lasts six years, after which a year must be spent in basic resident posts in recognised hospitals. Then there follow two years' compulsory National Service. If to this were added four additional years prescribed in detail, as was proposed, it would have meant that for thirteen years, from the age of, say, 18 to 31, the experience of all those entering a particular kind of post in the Health Service would tend to have been exactly alike. To appreciate the full significance of this, you must remember that in Great Britain there is now no career in clinical medicine outside the National Health Service. The example which showed up the folly of such proposals was mental health. In our National Health Service, mental health is the third most numerous specialty after general medicine and general surgery. It is also the most stagnant. It would seem abundantly clear that, if progress is to be made in this difficult field, every encouragement must be given to men of original mind, and with a great variety of experience of other branches of medical science. There could be no surer method of preventing such a development than by the establishment of regulations such as I have described.

It is quite beyond my capacity as a sociologist to trace the causes of this excessive appetite for legislation and regulation. In Great Britain, it is no doubt related to the concept of the Welfare State which grew out of the tragedy of unemployment between the wars, and the enormous and temporarily necessary growth of detailed centralised administration during the war. But there is undoubtedly a strong movement to introduce more uniformity into our educational system because, it is argued, education confers privilege, and privilege should be abolished.

## THE EXCEPTIONAL

In education there tends to be a fundamental difference of outlook between the administrator and the teacher. The administrator is concerned with rules and regulations that apply to large numbers of individuals.

*Abridged from the convocation address delivered to the American College of Physicians on April 27, 1955. Published by permission of the Editors of the *Annals of Internal Medicine*, in whose November issue the address appears in full.

1. *Observer*, Feb. 20, 1955, p. 7.

To deal with large numbers, one must assume that they have certain common properties, and there is no doubt in my mind that the administrator wants to believe, and in time tends to come to believe, that all students should be more or less alike and, if they are not, then they should be made so. The educationalist, on the other hand, is interested in individuals. He delights in the exceptional creature who often has great virtues and great faults. The function of the teacher is to develop the virtues and minimise the faults of his pupil and to direct the student into a channel of endeavour where his virtues will shine and his faults be unimportant. The conflict between the administrator and the educationalist is very similar to that between the farmer and the gardener, between the ready-made and the made-to-measure tailor. In contemporary societies with their huge populations and their urge to ever higher standards of living in a material sense, nothing can stop the development of a standardised product of high quality in large numbers. But I would like to urge that we should exercise great care lest the individual be lost in the process. And I would urge that this is particularly important in the field of higher university education, from which are likely to be recruited most of the leaders of our society and of our professions.

There is an important issue here which Sir Richard Livingstone has called the pursuit of the first-rate. I believe that society will be the poorer if we cease to allow, much less to encourage, that handful of rather odd creatures to fulfil their possible destiny. For, most of those who make important contributions to knowledge and ideas have had rather peculiar careers. The proposed regulations to which I have referred would have prevented James Mackenzie from obtaining a post as physician in the National Health Service, and while, as we know, his great scientific work was done in general practice, his influence on the next generation was more personal; and my late teacher, Sir Thomas Lewis, himself a peculiar creature, might not have done what he did had he not fallen under the influence of Mackenzie after his appointment to the London Hospital.

## The Growth of Knowledge

The next group of disorders springs from the growth of scientific and technological knowledge. If you agree with me that the disorders exist, then you will also agree that, unless we apply the appropriate remedies soon, the disorders will become serious before many more years, since scientific and technological knowledge seem to increase in geometrical progression.

### CURRICULA

The first disorder is overcrowding of the curriculum. In our country this is particularly true of medicine, technology, and science. It is less true in arts. In medicine, for example, not only new knowledge, but new subjects, are constantly being added to the curriculum. Rarely, if ever, is anything taken away. The student has to work increasingly hard to cover the ground, and he learns to appreciate those teachers and textbooks which provide him with knowledge in a form that can readily be reproduced for examination purposes. He has less and less time to devote to those aspects of civilised life which are not embraced within the confines of his curriculum.

This has two unfortunate consequences.

The first is educational. In the kind of teaching we give in universities, a distinction may properly be drawn between the processes of education and instruction. In education, the student is encouraged to work and think for himself; the function of the teacher is to stimulate and criticise. Education is expensive in time and effort of both teachers and taught. But it produces the most finely trained minds. By contrast, instruction is a process whereby the student is required to assimilate a series of dicta, without inquiring into their validity or necessarily considering the evidence on which they are based. It is a process which does not necessarily improve the mind of the recipient; and may actually do harm by suppressing curiosity, insight, and the capacity to learn from experience. Now, it is evident that overcrowding of the curriculum can have only one result—namely, that education gives place to instruction. I am one of those who still think that it would be better to send out our students knowing rather less, but understanding better how to learn, for the stock of facts with which they have been equipped is a steadily diminishing asset; and if they have not learned from us how to learn, then perhaps they never will.

Less obvious, but no less important, is the restriction imposed by an overcrowded curriculum on the pursuit of general cultural interests. If a student spends nearly all his day in receiving instruction and his evenings in working at his books it is not surprising that he is all too often uninterested in art, music, and literature, and in those intangible spiritual values on which ultimately any civilisation rests; in fact, in the finer products of the human mind. One of the qualities that is most essential in a doctor is wisdom and wisdom is acquired neither from instruction nor from textbooks. It is a product of two other qualities—a sense of proportion and an appreciation of ends. Both of these are qualities of the mind that can only be developed by personal experience. Personal experience requires time, which tends to be increasingly occupied with the narrower requisites of the curriculum. From the broader point of view, this would seem to me to be a serious disorder. The greatest danger to mankind arises from man himself, and wisdom is necessary today as it never was before.

### THE FASCINATION OF MACHINES

The second disorder arising from the growth of science and technology may be termed the fascination of machines. This disorder is one which manifests itself with unusual clarity in the field of medicine. As year succeeds year, some new physical or chemical technique, and some new and elaborate machine, is applied to the study of disease; great claims are always made for the precision of the answers yielded by these techniques and machines. One of the greatest struggles that a practising doctor has is to keep up to date with advances of this kind. No sooner has he mastered one than another is upon him. Moreover, the machines or techniques are often so complex that he cannot understand them. He has to take what they tell him on trust. It must be within the experience of many of us that there is a growing tendency for doctors to rely on the information given by such techniques and machines in preference to the information which they gain themselves from the history and physical signs. I am extremely doubtful if this is in the interests of good doctoring, and for three reasons. First, the errors and limitations of these new techniques are not at first appreciated. Often the data yielded by clinical examination are of much greater precision in the identification of disease. Second, a thorough clinical examination, which will only be carried out by doctors who appreciate its worth, is the best method of establishing that spirit of mutual understanding and good will which is the core of the doctor-patient relationship. Finally, to rely on data, the nature of which one does not understand, is the first step in losing intellectual honesty. The doctor is peculiarly vulnerable to a loss of this kind, since so much of therapeutics is based on suggestion. And it naturally leaves him and his patients the poorer.

There is another aspect of this question which deserves a little notice. For some years, it has been my privilege to visit institutions of learning with a view to deciding what financial help they need, and can profitably use.

There is no doubt that a collection of elaborate machinery makes a deep impression on the layman. It is necessary to be constantly on guard to see that support goes to men and ideas and not to machines.

### THE FRAGMENTATION OF KNOWLEDGE

The third disorder arising from the growth of science and technology is the fragmentation of knowledge. Existing knowledge is now so vast, and the techniques that are used to win new knowledge so exacting, that men are forced to canalise their efforts into a restricted compass.

So far as the practice of medicine is concerned, we are witnessing the extinction of the family doctor and even the general physician, and their replacement by a panel of specialists amongst whom the psychiatrist may seem to qualify best for the rôle of guide, philosopher, and friend. I am old-fashioned enough to think that something of inestimable value to the patient is lost in this process, and that there is a place for the old type of family doctor and for the general physician, as well as for the specialist. And I am glad to say that in Great Britain, there is a new movement to establish the prestige, and to define the peculiar functions, of the general practitioner or family doctor.

The other local symptom of this disorder is the steady addition to the medical curriculum of new subjects, each presided over by an autonomous professor. This process is, of course, necessary for the growth of knowledge. But, unfortunately, it tends to happen, in our country at least, that each professor feels it his duty to his subject to see that sufficient hours are allocated to it in the curriculum and that his subject has a separate examination in which the student must pass before he is allowed to leave that department. In my more detached moments, I see these worthy gentlemen, each determined to exact his pound of flesh, like a flock of vultures descending on the student, until only the bare bones are left. And I sometimes feel when I listen to these eminent scientists that their arguments are all perfectly valid, except that they have forgotten one thing—that the subject of their improving exercises is a living, feeling, and, we hope, thinking, human being whose capacity to take intellectual punishment is extremely limited. Nowadays, be it in medicine, be it in education, be it in political reform, there seems to be a tendency to forget the individual.

### THE TYRANNY OF JARGON

I come now to the last type of disorder, the tyranny of scientific and technological jargon. That this is a general disorder of contemporary society is well known, and Sir Winston Churchill has not spared his tongue on the kind of technical jargon used in the Civil Service. But I would venture to suggest that this disorder finds its most florid expression in the world of science and technology and particularly in the world of medicine.

To begin with, it is beyond dispute that a new element or a new compound must be given a name so that men may know it; so must a newly discovered process or force, or a new disease. Much of this technical jargon is, therefore, unfortunately necessary. It is an essential part of the growth of science and technology. But much of technological jargon is not really necessary and could easily be discarded. Technological jargon has two evil effects; first it accentuates the fragmentation of knowledge, and, second, it facilitates confusion of mind because it tends to hide it. I fancy that all of you have had a similar experience to my own, in finding difficulty in understanding what I read in some medical journals; I find greater difficulty in reading journals devoted to biochemistry, chemistry, botany, zoology, or genetics, and I find most mathematical or physical journals quite impossible. Some of this difficulty is due to new discoveries and new ideas since I was a student and some of my own defective education. But most is due to the use of unnecessary technological jargon. In creating our own jargon, we are fencing off our subject, so that it shall be, as it were, inaccessible to any not initiated into its technicalities.

If we are interested in the growth of knowledge, and if we acknowledge, as we must, that knowledge is a whole, then we must deplore anything that accentuates this process of fragmentation. We should, in fact, demand that technological words are never used in scientific papers if familiar words can be used instead. To give an example, I showed my colleague, the Professor of Anatomy, the following passage: "hypokalæmic hypochlorræmic alkalosis was present." He had no idea what is meant. Had the statement read: "plasma potassium and chloride were diminished, $CO_2$ increased," he would have understood. Here the simpler phrase is seven letters more. But editors are not always so particular in curbing verbosity. Moreover, another example from a recent paper by a very able and highly cultured author: "bilateral nephrectomy was performed," is not only less easy for a non-biological scientist to understand than: "both kidneys were removed," but is eleven letters longer. Much of this technological jargon is thus unjustifiable on any grounds whatsoever, and I can only regard it as a bad habit into which we all tend to fall.

The other evil consequence of technological jargon is not less important, but its ill effects are more insidious, and most of us, to a greater or less degree, are already its victims. I refer to its inhibitory effect on our own mental processes. When we use a technological term, there is a strong tendency for the idea to become isolated and inaccessible to those periodical spring-cleanings to which we subject our more ordinary mental furniture. Thus, by using a technological term, we often assume an entity where in fact none exists; the next process is to invent it. Thus, by using a technological term, we may create an artefact. An outstanding example of this is essential hypertension. The realisation that this condition is not an entity but merely represents one end of a curve of continuous variation, and thus that the condition is, in a sense, an artefact, has been one of my greatest personal experiences. Certainly many of the features that were said to characterise the course of the disease, and some of the more credible hypotheses of its causation were consequences not so much of facts but of the assumption made in interpreting them; the particular assumption made was that a dividing line could and should be drawn between normal blood-pressure and hypertension. This assumption was a consequence of the idea that essential hypertension was an entity, an idea that in its turn arose from the use of a technological term and the necessity to define it. In terms of wasted effort, the use of this technological term must have cost medical science several thousand man-years of mis-directed effort.

An important source of confusion arising from the use of technological terms is that they may seem to be much more precise than they are, and different people using the same word may be considering totally different things. This is well seen, for example, in the various uses of the words "stress" and "arteriosclerosis."

I would therefore advocate two things: first, that we should watch very carefully our own use of technological jargon; and, second, that we should not allow our students and assistants to use it unless they can explain to us in simple words what they mean by the terms they employ. If we do this, I have little doubt that our pupils will in the long run have reason to be grateful to us. My personal contacts with great scientists leads me to suppose that one of the reasons they have made their great contributions is because the ideas and images which they manipulate in their minds are relatively

simple and well-defined and bear a close relation to reality. I would suggest that the greatest enemy to straight thinking in medicine is technological jargon.

In trying to give you a brief description of these disorders of society, which seem particularly to obtrude in the world of medicine, I am aware of two grave defects—that I have omitted important disorders and that I have not considered prognosis and treatment. Thus I have omitted a very grave disorder now assuming the proportions of a major epidemic in Great Britain—namely, an excessive appetite (or is it a perverted appetite?) for committes, which is so effective in reducing the productivity of our best minds. With regard to prognosis, I have nothing useful to say. With regard to treatment, I would doubt whether we need await a new antibiotic or some new application of nuclear fission. I may be wrong, but I suspect that these disorders would respond readily to that old-fashioned but none-the-less potent remedy, the application of common sense.

## ACUTE RENAL FAILURE ASSOCIATED WITH CONCEALED ACCIDENTAL HÆMORRHAGE OF PREGNANCY

G. M. BULL
M.D. Cape Town, F.R.C.P.
PROFESSOR OF MEDICINE IN THE QUEEN'S UNIVERSITY OF BELFAST

A. M. JOEKES
M.A., B.M. Oxfd, M.R.C.P.
SENIOR MEDICAL REGISTRAR, ST. MARY'S HOSPITAL, LONDON

K. G. LOWE
M.D. St. And., F.R.C.P.E., M.R.C.P.
LECTURER IN MEDICINE IN THE UNIVERSITY OF ST. ANDREWS

IN reviewing all our patients with anuria or severe oliguria we have divided them into clinical groups in which acute renal failure followed such different causes as intravascular hæmolysis (particularly due to a mismatched blood-transfusion), poisoning with mercury or other nephrotoxic agent, criminal abortion, concealed accidental hæmorrhage of pregnancy, &c.

We review here 22 patients in whom renal failure followed concealed accidental hæmorrhage. All 22 had the typical clinical course of this complication of the last trimester of pregnancy as described by Sheehan and Moore (1952). We have, however, departed from the strict criteria of these authors in one respect: 3 of our patients had a live child despite placental infarction with retroplacental blood-clot and, in at least 2 of them, uterine subperitoneal hæmorrhage. None of our patients had placenta prævia or rupture of the lower uterine segment. None of those receiving emergency blood-transfusion were thought to have hæmolytic transfusion reactions.

Tables I and II give details of the 18 patients who recovered and table III details of the 4 fatal cases. Table I shows all the cases of concealed accidental hæmorrhage of pregnancy that occurred in the two teaching hospitals of Dundee in two years. All the patients had some upset of renal function, varying from very mild to moderately severe, and all recovered with simple conservative management. Cases 1–7 (table I) had short-lived suppression of excretion of urine, usually only for several hours; proteinuria for several days; and peak blood-urea levels of 25–82 mg. per 100 ml. The 6 other patients (table II) were all seen in consultation in hospitals other than our own, and only 1 of them was transferred to our care at Hammersmith Hospital. These 6 patients and cases 8–12 had moderate or severe renal failure with oliguria lasting from two to ten days and peak blood-urea levels of 120–450 mg. per 100 ml. All made a satisfactory clinical recovery on conservative treatment.

These 18 patients (tables I and II) were thought to have renal damage proportional to the disturbance of renal function as shown by duration of oliguria and rise in blood-urea level. Their oliguria was not due to underhydration. The mildest cases—e.g., cases 3 and 7 (see table I and figs. 1 and 2)—probably would at the most show only trivial kidney damage. The more severe cases would probably show either acute tubular necrosis or incomplete cortical necrosis. Necropsy in the 4 fatal cases (table III) showed gross cortical necrosis incompatible with clinical recovery. The first 2 deaths, on the sixth and eleventh days, although inevitable, were accelerated by overloading with salt and water.

The following case-reports illustrate the clinical spectrum of severity of renal failure.

TABLE I—ACUTE RENAL FAILURE FOLLOWING CONCEALED ACCIDENTAL HÆMORRHAGE OF PREGNANCY

| Case no. | Age (yr.) | Previous obstetric history | Present pregnancy | | | | | | | | Day of 1 litre diuresis | Highest blood-urea (mg. per 100 ml.) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Toxæmia | Duration (days) | On admission | | Lowest Hb % | Emergency blood-transfusion (pints) | Duration of labour | Days of oliguria <300 ml. per day | | |
| | | | | | B.P. (mm. Hg) | Hb % | | | | | | |
| 1 | 35 | 6 normal pregnancies | No | 251 | 90/60 | .. | 47 | 2 | 9 hr. 20 min. | 0 | 2 | 25 |
| 2* | 37 | 1 stillbirth (fœtal abnormality); 1 normal pregnancy; both by cæsarean section | Yes | 256 | 175/95 | .. | 58 | 1 | 3 hr. | 0 | 1 | 30 |
| 3 | 23 | 1 normal pregnancy | No | 211 | 160/95 | 52 | 50 | 2 | 15 hr. 45 min. | 0 | 1 | 48 |
| 4 | 27 | 1 normal pregnancy | No | 225 | 124/90 | 68 | 62 | 1 | 9 hr. 10 min. | 0 | 1 | 48 |
| 5 | 24 | 1 pregnancy: toxæmia; stillbirth | Yes | 247 | 130/100 | 68 | 62 | 1 | 10 hr. 50 min. | 1 | 3 | 54 |
| 6 | 46 | 5 normal pregnancies | No | 270 | 120/70 | .. | 47 | 2 | ? | 0 | 7 | 66 |
| 7 | 42 | First pregnancy, cæsarean section for ? contracted pelvis; 9 subsequent normal pregnancies | No | 233 | 95/65 | 38 | 38 | 4 | 5 hr. | 1 | 7 | 82 |
| 8 | 29 | Nil | No | 236 | 100/65 | .. | 58 | 2½ | 12 hr. 55 min. | 2 | 4 | 120 |
| 9 | 37 | 8 normal pregnancies | No | 256 | 98/60 | 34 | 34 | None | 16 hr. 50 min. | 3 | 4 | 228 |
| 10† | 41 | 7 normal pregnancies | No | ? | 130/80 | 45 | 45 | 4 | ? | 3 | 6 | 268 |
| 11 | 31 | 1 normal pregnancy: 1 abortion | No | 236 | 155/100 | .. | 45 | None | 10 hr. 20 min. | 2 | 4 | 274 |
| 12 | 30 | 2 normal pregnancies | No | 251 | 115/80 | 55 | 30 | 3 | 12 hr. | 4 | 8 | 274 |

* Cæsarean section, live birth, uterine subperitoneal hæmorrhage. † Live child.

TABLE II—ACUTE TUBULAR NECROSIS OR INCOMPLETE CORTICAL NECROSIS FOLLOWING CONCEALED ACCIDENTAL HÆMORRHAGE OF PREGNANCY

| Case no. | Age (yr.) | Previous obstetric history | Present pregnancy | | | | Days of oliguria (<300 ml. per day) | Day of 1 litre diuresis | Highest blood-urea (mg. per 100 ml.) |
|---|---|---|---|---|---|---|---|---|---|
| | | | Toxæmia | Duration (days) | Admission B.P. (mm. Hg) | Emergency blood-transfusion | | | |
| 13 | 41 | 1 pregnancy complicated by toxæmia; 1 miscarriage | ? | 185 | 140/80 | None | 2 | 3rd | 120, 7th day |
| 14 | 30 | 1 normal pregnancy; 1 miscarriage | No | 185 | 110/70 | Yes | 3 | 4th | 128, 7th day |
| 15 | 30 | 1 pregnancy complicated by toxæmia | Yes | ? | ? | None | 6 | 8th | 236, 7th day |
| 16 | 34 | 1 normal pregnancy | No | 184 | 80/60 | 2 pints | 4 | 8th | 253, 9th day |
| 17 | 30 | 1 normal pregnancy | Yes | 239 | 150/110 | None | 6 | 8th | 290, 11th day |
| 18 | 33 | 1 normal pregnancy | Yes | 241 | 110/90 | None | 10 | 13th | 450, 14th day |

TABLE III—FATAL CORTICAL NECROSIS FOLLOWING CONCEALED ACCIDENTAL HÆMORRHAGE OF PREGNANCY

| Case no. | Age (yr.) | Previous obstetric history | Present pregnancy | | | | Days of oliguria (<300 ml. per day) | Highest blood-urea (mg. per 100 ml.) | Remarks |
|---|---|---|---|---|---|---|---|---|---|
| | | | Toxæmia | Duration (days) | Admission B.P. (mm. Hg) | Emergency blood-transfusion | | | |
| 19 | 32 | Nil | Yes | 251 | 210/120 | None | 6 | 316 | Died from pulmonary œdema after treatment with artificial kidney |
| 20* | 35 | 6 normal pregnancies | Yes | 236 | 186/134 | None | 11 | 213 | Died from pulmonary œdema due to excessive administration of water and salt |
| 21† | 24 | Nil | Yes | 199 | 160/120 | None | 28 | 292 | Treatment with artificial kidney at weekly intervals |
| 22 | 30 | Not known | Yes | 208 | 230/120 | None | 42 | 485 | Conservative management only |

* Twin delivery (one live, one stillborn). † Reported previously (Jockes and Bull 1948).

## Case-reports

**Case 3** (see table I and fig. 1).—Last menstrual period (L.M.P.) Oct. 31, 1951. Expected day of confinement (E.D.C.) Aug. 7, 1952. At her last antenatal-clinic attendance on July 27, 1952, no abnormality was noted. At 4.45 P.M. next day she had a sudden onset of severe abdominal and low back pain, faintness, and vomiting. Admitted early next morning. Pulse-rate 84. Blood-pressure (B.P.) 165/105 mm. Hg. Pale; no œdema; uterus tense, hard. Gross proteinuria. There was frank revealed hæmorrhage at 4.35 A.M. on July 29, 1952, and 2 pints of blood was transfused. The membranes ruptured spontaneously at 8.20 A.M. and a stillborn fœtus was delivered by 8.32 A.M. The placenta was infarcted, with retroplacental blood-clot. During the next 24 hours she passed 1200 ml. of urine, and her blood-urea level that day was 48 mg. per 100 ml. She made a rapid clinical recovery, and there was no evidence of residual kidney damage.

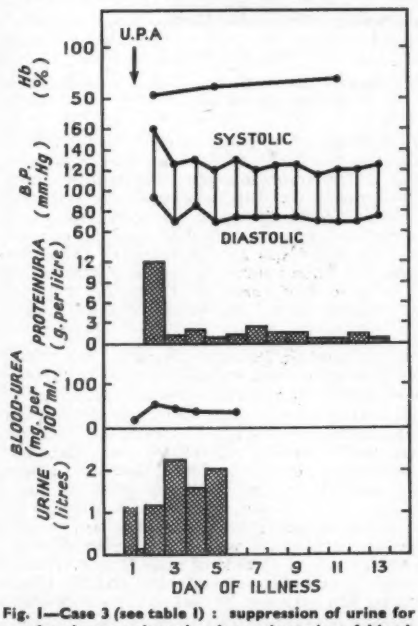



**Fig. 1—Case 3 (see table I): suppression of urine for a few hours only and only a minor rise of blood-urea level.* U.P.A., uteroplacental apoplexy (concealed accidental hæmorrhage of pregnancy).**

* Blood-urea level is assumed in this and the following figures to have been normal before onset of bleeding.

**Case 7** (see table I and fig. 2).—L.M.P. Aug. 26, 1952. E.D.C. June 2, 1953. Admitted on April 15, 1953, after painless antepartum hæmorrhage. On examination: "shocked"; pulse-rate 90; B.P. 95/65 mm. Hg. Uterus tense and tender; absence of fœtal heart sounds. Hæmoglobin 38%. 4 pints of blood was transfused and a stillborn fœtus was delivered spontaneously five and a quarter hours after the onset of the vaginal bleeding. The placenta was found completely separated by blood-clot. Clinical recovery was rapid; proteinuria lasted five days, and the blood-urea level had returned to normal in the second week, the peak being 82 mg. per 100 ml. on the sixth day.

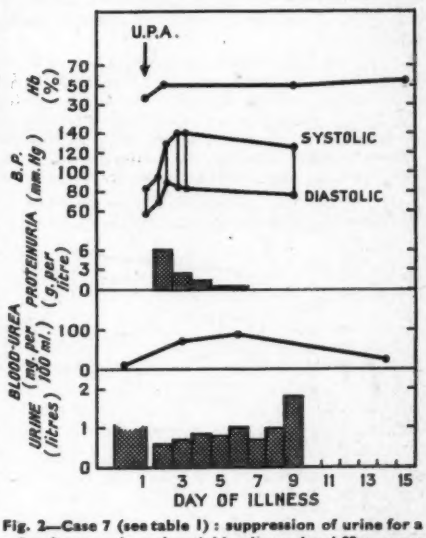



**Fig. 2—Case 7 (see table I): suppression of urine for a few hours only and peak blood-urea level 82 mg. per 100 ml.**

**Case 9** (see table I and fig. 3).—L.M.P. Sept. 19, 1951. E.D.C. June 26, 1952. Attended antenatal clinic on April 2, 1952 (B.P. 135/80 mm. Hg; urine, no abnormality; no œdema). At 11.30 A.M. on June 26, 1952, she had a sudden onset of severe abdominal and low back pain, faintness, and vomiting.

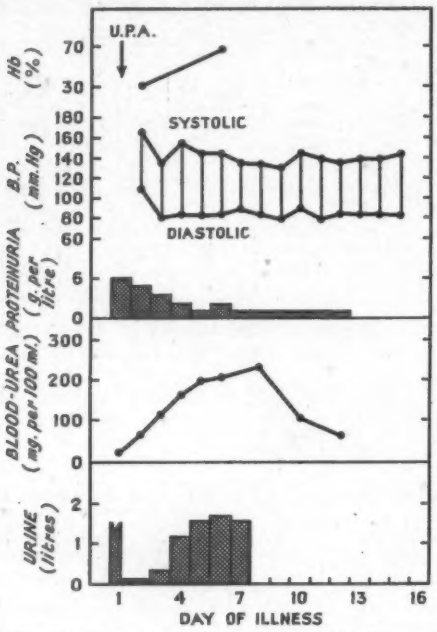



**Fig. 3—Case 9 (see table I): oliguria for about 3 days; moderate azotæmia.**

The pain lessened at about 5.30 P.M., when vaginal bleeding started. On examination: pale; "shocked"; skin "cold and clammy." B.P. 98/60 mm. Hg (rising to 165/110 mm. Hg during labour); uterus "wooden hard"; no œdema. June 27, 1952, delivered of stillborn fœtus; placenta infarcted and "ploughed-up"; retroplacental clot. Low-protein high-calorie oral diet with approximate salt and water balance. Satisfactory diuresis on fourth day followed by rapid clinical recovery. Peak blood-urea level 228 mg. per 100 ml. on the eighth day.

**Case 11** (see table I and fig. 4).—L.M.P. Sept. 21, 1952. E.D.C. June 29, 1953. She had been under routine antenatal supervision by own doctor. At 4 P.M. on May 14, 1953, she had a sudden onset of abdominal pain and haziness of vision; some six hours after, while in ambulance, she had severe vaginal bleeding. On admission: "shocked"; B.P. 155/100 mm. Hg; uterus tense and board-like; absence of

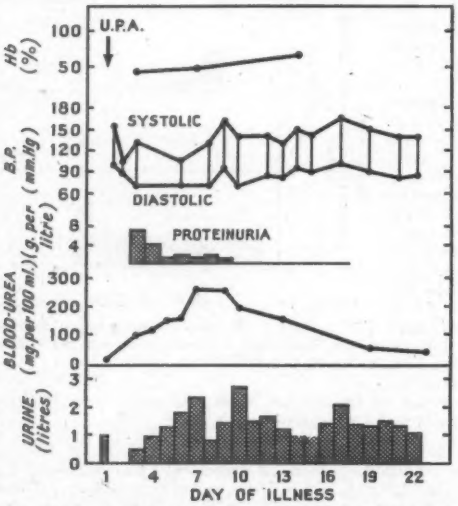



**Fig. 4—Case 11 (see table I): oliguria for about 2 days, peak blood-urea level 274 mg. per 100 ml.**

fœtal heart sounds; transverse lie. At 2.10 A.M. on May 15, 1953, internal version was done, and stillborn fœtus was delivered at 2.20 A.M. The placenta was complete, but retroplacental clot was present. No urine was passed that day, but subsequently the urine flow increased, and she passed more than a litre on May 18, 1953. The peak blood-urea level was 274 mg. per 100 ml. on the seventh day. Treatment was with oral low-protein high-calorie diet with approximate salt and water balance, and a satisfactory clinical recovery was made.

**Case 12** (see table I and fig. 5).—L.M.P. Dec. 3, 1951. E.D.C. Sept. 9, 1952. Patient had been in good health, and no abnormality had been noted at routine antenatal visits to her own doctor. At 2.30 A.M. on Aug. 11, 1952, she had a sudden onset of vomiting and brisk, vaginal hæmorrhage. On examination some hours later: "shocked"; sweating; pulse-rate 90; B.P. 115/80 mm. Hg; slight ankle œdema; uterus hard and tense. Transfused 3 pints of blood. Artificial rupture of membranes at 8.30 A.M. and spontaneous delivery of stillborn fœtus at 2.35 P.M. Retroplacental blood-clot present. Gradual diuresis, and on eighth day passed more than a litre of urine. Peak blood-urea level 274 mg. per 100 ml. on ninth day. Treatment was with oral low-protein high-calorie diet and approximate salt and water balance, and a good clinical recovery was made.

**Case 17** (see table II and fig. 6).—L.M.P. July 8, 1948. E.D.C. April 15, 1949. Emergency hospital admission on March 5, 1949. During the previous week she had been in bed on account of raised blood-pressure, œdema, and albuminuria, and on the day of admission she complained of severe abdominal and low back pain, headache, vomiting, blurred vision, and slight vaginal

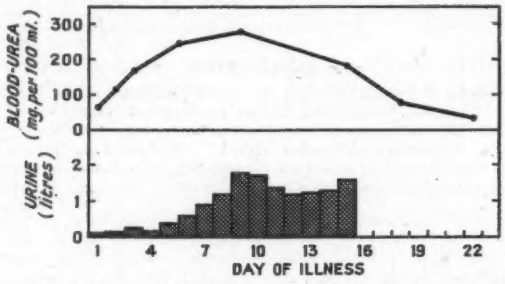



**Fig. 5—Case 12 (see table I): oliguria for 4 days; peak blood-urea level 274 mg. per 100 ml.**

bleeding. On examination: pale; facial œdema; B.P. 150/110 mm. Hg; uterus hard and tender. Heavy proteinuria. Six hours after admission she was spontaneously delivered of a stillborn fœtus. Retroplacental blood-clot was present. She was tube-fed a fat-sugar emulsion (Bull et al. 1949) for six days and subsequently had oral low-protein high-calorie diet. She was anuric for three days and then had a gradual diuresis, her urine volume exceeding a litre on the eighth day. The peak blood-urea level was 290 mg. per 100 ml. on the eleventh day. She made a good clinical recovery.

**Case 18** (see table II and fig. 7).—L.M.P. April 9, 1949. E.D.C. Jan. 16, 1950. Emergency admission on Jan. 8, 1950, on account of sudden onset of abdominal pain, followed two hours later by vaginal bleeding. During the preceding two weeks she had had increasing œdema, transient blurring of vision, and oliguria. On examination: pulse-rate 72; B.P. 110/90 mm. Hg; cold extremities; generalised œdema; tense uterus. Heavy proteinuria. She was delivered of a stillborn fœtus six and a half hours after the onset of abdominal pain. About 6 oz. of old blood-clot followed immediately after delivery, and the maternal surface of the placenta was covered with adherent blood-clot. She had a severe episode of renal failure, diuresis being delayed until the end of the second week, and the blood-urea level rising to 450 mg. per 100 ml. on the fourteenth day. Treatment was by tube-feeding of fat-sugar emulsion. During the oliguric period her condition gave rise to some anxiety on account of drowsiness, twitching, blurring of vision, and transient congestive heart-failure. On the sixteenth day she was able to take oral low-protein high-calorie diet. After the end of the third week of illness she had a rapid and satisfactory convalescence.

**Case 22** (see table III and fig. 8).—L.M.P. April 27, 1954. E.D.C. Feb. 1, 1955. Not under medical supervision. On Nov. 20, 1954, noticed swelling of hands and legs, absence of fœtal movements, abdominal pain, and the passage of blood-clot per vaginam. Admitted to Jubilee Hospital, Belfast, under the care of Mr. W. S. Campbell. B.P. 230/120 mm. Hg. Oliguric. Urine: protein ++, blood ++. Two hours after admission delivered of stillborn fœtus. Placenta "ragged and unhealthy"; retroplacental clot. Hæmaturia continued for two days, but the renal tenderness was not more marked than might be expected after normal delivery. She was treated conservatively by the tube-feeding régime. On the twenty-fifth day she was transferred to the Royal Victoria Hospital, Belfast, because mild signs of water intoxication had developed. This biochemical upset was corrected by conservative management. No dialysis was used at any time. Consciousness was only lost in the last week of illness, when a chest infection developed. She died on Jan. 1, 1955, on the forty-second day of illness. The greatest daily urine volume was 700 ml. on the thirty-fourth day. At necropsy extensive bilateral renal cortical necrosis was found. Owing to the long survival period considerable resorption of the necrotic tissue had taken place and fibrosis was starting. The average thickness of the renal cortex was about 2 mm.

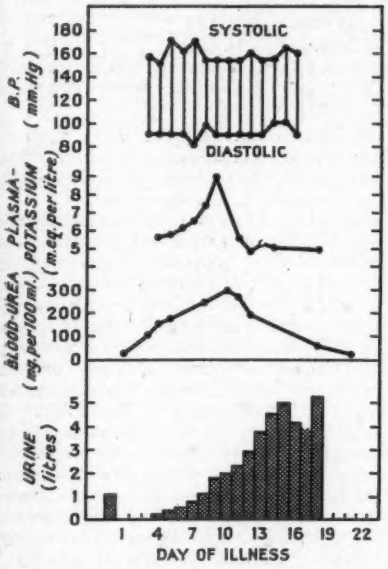



**Fig. 6—Case 17, aged 30: concealed accidental hæmorrhage complicating toxæmia of pregnancy, showing typical course ending in clinical recovery under conservative treatment.**

## Discussion

Our clinical and laboratory data in these 22 cases showed clearly the gradation in severity of renal failure that may follow concealed accidental hæmorrhage. It was impossible to relate the severity of the renal lesion to such factors as age, parity, amount of concealed or overt blood-loss, and duration from onset of bleeding to delivery. The 4 patients with cortical necrosis, however, had more severe signs of toxæmia and higher blood-pressure on admission than had any of the 18 patients who recovered. Though a severe renal lesion may result from concealed accidental hæmorrhage in the absence of toxæmia, those patients with renal cortical necrosis are perhaps more likely than not to have had severe pre-existent toxæmia.

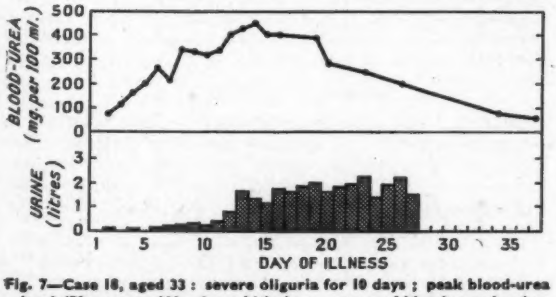



**Fig. 7—Case 18, aged 33: severe oliguria for 10 days; peak blood-urea level 450 mg. per 100 ml. on 14th day; return of blood-urea level to normal in 6th week of illness.**

From necropsies of 67 patients who died after concealed accidental hæmorrhage of pregnancy Sheehan and Moore (1952) demonstrated a gradient in severity of the associated renal lesions. In the mildest cases of renal damage there were only protein precipitate and protein casts in the tubular lumina. There then followed a series of increasingly severe degenerative changes in the tubular epithelium (which we call "acute tubular necrosis") and, finally, renal cortical necrosis, graded in order of increasing severity as focal, minor, patchy, and gross. Our present series of cases of acute renal failure form a clinical counterpart to Sheehan and Moore's necropsy series.

Renal-clearance and other biochemical tests were made on some of these patients and on other patients with acute renal failure due to causes other than concealed accidental hæmorrhage. These data have been reported elsewhere (Bull et al. 1950, Lowe 1952, Lowe et al. 1954). The pattern of disturbed renal function in acute tubular necrosis due to concealed accidental hæmorrhage is similar to that in acute tubular necrosis due to any other disturbance of the general circulation or to poisoning—e.g., mercury and phenol.

Many patients with acute renal failure following concealed accidental hæmorrhage never had a low blood-pressure; in fact, it may remain at hypertensive levels throughout the illness. Such patients have pallor, sweating, and rapid pulses and are described clinically as shocked. There is probably generalised vasoconstriction

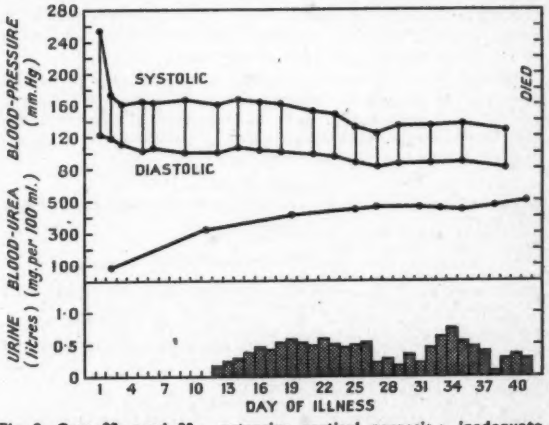



**Fig. 8—Case 22, aged 30: extensive cortical necrosis; inadequate diuresis and death in uræmia on 42nd day under conservative treatment.**

but most severe and most harmful in the renal vascular bed. It is therefore possible that more extensive use should be made of various techniques of renal sympathetic block in the early phase of acute renal failure (Barry et al. 1955). Observations on renal function before and after renal sympathetic block would be valuable.

As regards treatment, we have departed from our original régime (Bull et al. 1949) in several respects. Patients with very mild acute renal failure need practically no dietary restrictions or, at the most, should be treated like patients with acute nephritis with oral low-protein high-calorie diet and approximate salt and water balance. When diuresis is delayed for more than twenty-four to forty-eight hours, strict attention to diet is required. The original tube-feeding régime of fat-sugar emulsion is still useful for some patients. We prefer to allow only about 500 ml. of water a day for insensible water-loss and attach much less importance to the inclusion of fat in the diet. Supplementary use of sodium-charged

cation-exchange resin, either orally or by retention enemata, is sometimes required as an additional measure to prevent potassium intoxication (Elkinton et al. 1950, Bull 1952, Evans et al. 1953). Tube-feeding the fat-sugar emulsion is often poorly tolerated because of nausea, vomiting, diarrhœa, or retrosternal discomfort. Like other workers in this field (De Keyser et al. 1949, Russell et al. 1954, Shaw and Mair 1954) we have therefore gradually gone over to the use of intravenous hypertonic glucose infusion into either the superior or the inferior vena cava as an alternative to tube-feeding in the very severe cases of acute renal failure. The additional use of dialysis (particularly the modern highly developed artificial kidney handled by an expert team) is occasionally indicated, but its routine use is controversial. Correction of such chemical disturbances as acidosis and hyponatræmia may at times be desirable, but the calculated amounts of the requisite salts should be given cautiously. For fuller discussion of treatment in uræmia see Bull (1955).

Our knowledge of the ætiology, natural history, and best treatment of acute renal failure is far from complete, and much investigation is still required. Nevertheless much has been learnt in this field since the beginning of the last war. It is now possible to approach each clinical case with some optimism and rational methods of treatment and with the continued hope of furthering knowledge by clinical and biochemical investigation.

### Summary

As a clinical counterpart to the classical necropsy studies of Sheehan and Moore (1952) on renal failure following concealed accidental hæmorrhage of pregnancy, the case-reports of 22 patients are presented of whom 18 (with graded severity of renal failure) recovered and 4 (with gross renal cortical necrosis) died.

We are grateful to Prof. Margaret Fairlie and Miss Jean Herring for permission to study the Dundee cases, and to Mr. W. S. Campbell, Dr. E. G. L. Bywaters, Dr. Avery Jones, Dr. Gavin Shaw, and many other physicians and surgeons for referring or discussing their cases.

REFERENCES

Barry, A. P., Feeney, J. K., Geoghegan, F. J. (1955) *Brit. med. J.* ii, 12.
Bull, G. M. (1952) *Proc. R. Soc. Med.* **45**, 848.
— (1955) *Lancet*, i, 731, 777.
— Jockes, A. M., Lowe, K. G. (1949) *Ibid*, ii, 229.
— — — (1950) *Clin. Sci.* **9**, 379.
De Keyser, R., Van Eeckhoutte, P., Kop, P. S. M., Kolff, W. J. (1949) *Ned. Tijdschr. Geneesk.* **93**, 2386.
Elkinton, J. R., Clark, J. K., Squires, R. D., Bluemle, L. W., Crosley, A. P. (1950) *Amer. J. med. Sci.* **220**, 547.
Evans, B. M., Hughes-Jones, N. C., Milne, M. D., Yellowlees, H. (1953) *Lancet*, ii, 791.
Jockes, A. M., Bull, G. M. (1948) *Proc. R. Soc. Med.* **41**, 678.
Lowe, K. G. (1952) *Lancet*, i, 1086.
— Moodie, G., Thomson, M. B. (1954) *Clin. Sci.* **13**, 187.
Russell, C. S., Dewhurst, C. J., Brace, J. C. (1954) *Lancet*, i, 902.
Shaw, G., Mair, J. (1954) *Ibid*, p. 1031.
Sheehan, H. L., Moore, H. C. (1952) Renal Cortical Necrosis and the Kidney of Concealed Accidental Hæmorrhage. Oxford.

"... In general practice we are individuals conducting our own practices in our own individual ways, working directly with our own patients, and adapting our methods to their needs. I hope we will ever preserve this individuality even while we strive to adapt and absorb into our practices the great advances that modern research in medicine and in technicology offer for our advantage. . . . let me first state for myself as simply as I can what it is I feel that general practice holds that makes it satisfying to me. I think it is the opportunity it gives for doing things in my own way for my own patients, and for going on doing so, not at one special time, but through all their lives, not for one special ailment, but in all their illnesses and tribulations, getting to know them and their families, their homes, and their jobs, their habits and their fads—in fact, being their family doctor. I want to do as much as I can for them myself, but I realise that to do so I need a variety of help, help which can extend my usefulness to them. Finally, when they are beyond help I still want to offer what solace I may to them and to those who care for them."—Dr. A. Talbot Rogers, *Med. J. Aust.* Nov. 5, 1955, p. 753.

# PROTOPHRENIA

## A STUDY OF PERVERTED REARING AND MENTAL DWARFISM

HAROLD BOURNE
M.B. Lond., D.P.M.
LECTURER IN PSYCHIATRY, UNIVERSITY OF OTAGO MEDICAL SCHOOL, NEW ZEALAND; LATELY MEDICAL OFFICER, FOUNTAIN HOSPITAL, LONDON

THE purpose of this communication is to present briefly a hypothesis in psychopathology and its objective investigation, to outline the disease entity which emerges, and to indicate its frequency and importance.

The work was planned to determine (1) whether severe mental defect may result from social and psychological adversity in infancy—i.e., whether "psychogenic amentia" may be added to the types of mental defect already distinct[1]—and (2) to discover the prevalence and clinical features of psychogenic amentia if it really exists.

At the Fountain Hospital, with 600 beds for mentally defective children, almost all under 5 years old on admission, the processes causing severe mental defect are relatively recent and thus unusually accessible. It will be shown that clinically, as well as at necropsy (Crome 1954), most of the severe cases can be explained by organic brain disease, and that heredity seems much less significant than is sometimes believed. There remains a small group of children, lacking any apparent organic or familial pathology, who appeared to me to display notably both a curious pattern of abnormal behaviour and a background of appalling misfortune. It was postulated that in such cases a faulty upbringing might cause failure of mental growth.

It has become common knowledge, since Freud, that early experience may predispose to psychological disorder later. Hence it is conceivable that, when extreme enough, emotional trauma in infancy can also have immediate effects which completely disrupt the basic processes of mental development and thus induce gross defect. Clinical intuition has led to this view before—e.g., Klein (1932)—and scientific evidence for it already exists in the classical studies by Spitz (1945, 1946) and Goldfarb (1945) of retardation in institutional children.

Another consideration is that social influences are important in the occurrence and outcome of schizophrenia (Hollingshead and Redlich 1954, Wahl 1954), which in adults or children often proceeds to mental disorganisation indistinguishable from mental defect and also without any known cerebral pathology.

By artificial derangement of their early environment, it has been revealed that the "innate" skills and behaviour patterns of animals are not simply inborn as once was believed (Lorenz 1935). To develop them, animals require certain stimuli, normally always encountered by the species, and the absence of early exposure to appropriate social situations and objects may be followed by behaviour foreign to the species or by defect of "natural" abilities, such as nest-building (Promptov 1953). Biologically, therefore, it is reasonable to explore the clinical suspicion that mental dwarfism in man can follow distortion of infant experience.

### Method of Investigation

A survey was accordingly devised to show whether, in comparison with other mentally defective children, these children whose mental defect has no apparent organic cause come from an environment psychologically more unfavourable, and whether they do present clinically distinct behaviour.

1. A reminder may be useful, here, that "mental defect" is not a medical diagnosis in the ordinary sense but, like "insanity," a legal or social designation for the victims of many unrelated disease processes.

For the survey I investigated 154 cases admitted consecutively to the Fountain Hospital. Except at the beginning, when occasional new patients did not come under my care, this includes every admission during two years, apart from a dozen eliminated as unsuitable for reasons given below.

Two groups were distinguished—those with discernible organic disease, and those without. Then the psychological background and the behaviour of each were compared statistically. The clinical separation of the two groups was my own task; but the information needed to compare the social experience of the groups was collected from reports by very many other observers and is independent of any subjective bias of mine.

*Exclusion of Unsuitable Cases*

5 cases were eliminated for lack of data concerning their social history: 4 of these had obvious organic disease; and 1, possibly epileptic, stayed only a few hours. The little known about their background is in no way discrepant from the results of the survey.

Though mental dwarfism is pathological, subnormal intelligence need not be so, any more than is subnormal stature. In the general population the scatter of intelligence is wide, and only some individuals towards the lower limit require care under the Mental Deficiency Acts; when they do, it is not usually through feeble intelligence alone. Burt (1947) shows how the distribution of intelligence in normal and in defective children overlaps. The present work was a study of pathological processes, and to avoid dilution by children within the lower physiological range of intelligence those with an intelligence quotient (I.Q.) exceeding 50 were excluded. Intentionally this limit was low, since intelligence testing in young children is somewhat unreliable. Among the 7 children so eliminated, the I.Q. spread from 56 to 90, 5 had organic disease, and 2 were abandoned children. As it happened, including them would not materially have altered the results.

*Separation of Two Groups*

Of the 154 cases, 138 had an evident organic cause and 16 had none. The distinction was based on clinical investigation and a medical history derived from several sources. The chief source was standard history forms completed by the hospital's social workers in each case, and in 74 by the outpatient consultants as well. Also there were 330 medical reports—an average of 2 per patient in the larger group and 3 in the smaller—specially requested from hospitals attended previously. Many of these were really plural reports, concerning more than one admission, or coming from independent departments, or referring to other members of the family too; in 100 of the cases, including 14 of the smaller group, the pregnancy and labour were described. In 34 cases I interviewed relatives—mostly at their wish, but in a few cases to get extra details.

There were 36 deaths, all in the larger group, 31 coming to necropsy, and in all of these organic disease was found.

The clinical distinction was difficult only twice:

(1) A child, admitted at the age of $3^1/_2$ years from a disordered family in a rest centre, had no certain physical abnormality. Hydrocephaly was suspected from the skull contours, but the skull dimensions were normal. He died nine months later, and necropsy revealed the rare condition of megalencephaly, the brain weighing 1665 g. (normal 1200 g.).

(2) A physically healthy child, aged $3^1/_2$ years, had still as little mental organisation as in her first weeks of life. The mother related that the infant was born very blue, with the cord tightly round her neck, was resuscitated with great difficulty, and for some days seemed moribund. Though no medical report was available, the circumstances were convincing, and the case was ascribed to brain damage from anoxia at birth.

Table I lists the pathology of the "organic" group—90% of 154 cases. This figure is close to Penrose's (1938) finding that 83% of 655 more severely defective persons presented such conditions; and his material was 20 years older, on average, and so harder to unravel.

*Comparison of the Two Groups*

The information was gathered from the sources mentioned for the medical history, the standard forms ensuring certain items uniformly for all cases, and the reports from other hospitals supplying occasional psychiatric accounts of near relatives; in addition, there were 209 reports from outside social agencies, mainly local-authority workers.

Where occasional discrepancies were met, an obviously less reliable report was discarded, or further inquiry was made. My judgment replaced that of others in a single instance:

All accounts referred to a mother as mentally defective because she had been certified as such in prison and spent years in a colony. As her letters were far too fluent for this diagnosis, she was interviewed. She proved to be a psychopath, of at least average vocabulary and literacy, from a criminal family, and now the prosperous young widow of an engineer who had died "suddenly." If she was defective, it was in morals and not intelligence.

For statistical treatment, the social histories compiled in this way were tabulated, the items extracted for this falling into some fifty categories. The two groups were then compared statistically, item for item, mainly by the $\chi^2$ test with the Fisher-Yates correction, required because one group was numerically small.

Because the number of mongols in the organically affected group was large, it was necessary to prevent unknown factors that might be peculiar to them from influencing the comparisons, either by swamping real differences or by creating misleading ones. As a precaution, every calculation had to be repeated with mongols treated as an isolated group. In the event, this turned out to have been superfluous, uncovering nothing otherwise overlooked, and indicating only the differences to be expected between mongols and the rest of the organic cases. Therefore, except where mentioned, the results all refer to comparisons between the whole

TABLE I—CLINICAL FINDINGS IN THE "ORGANIC" GROUP OF 138 CASES

| *Pathological condition* | *No. of cases* |
|---|---|
| *Birth trauma:* | |
| Mechanical, with residual neurological disorder | 3 |
| Prolonged anoxia | 1 |
| Prematurity, prolonged anoxia, with total failure to thrive | 1 |
| *Congenital deformities* with other abnormality | 4 |
| *Epilepsy:* | |
| As sole disease | 14 |
| With other abnormality | 36 |
| *Eye disease* with other abnormality: | |
| Blind or nearly blind | 15 |
| Optic atrophy | 9 |
| Chorioretinitis | 1 |
| Microphthalmia | 3 |
| Congenital cataract | 2 |
| Total affected with any eye condition | 21 |
| *Gargoylism* | 1 |
| *Head injury as well as other ætiology* | 2 |
| *Hemiplegia with epilepsy* | 3 |
| *Hypopituitarism with other disease* | 1 |
| *Megalencephaly (necropsy diagnosis)* | 1 |
| *Meningitis:* | |
| Tuberculous | 2 |
| Other, with residual neurological disorder | 2 |
| *Meningocele with hydrocephaly* | 1 |
| *Mongolism* | 40 |
| *Neurological disorder, bilateral:* | |
| As sole abnormality | 2 |
| With microcephaly | 19 |
| With other disease | 22 |
| *Phenylketonuria* | 3 |
| *Rhesus encephalopathy with gross neurological disorder* | 5 |
| *Rickets with other disease* | 1 |
| *Skull deformity:* | |
| As sole disease | 2 |
| With other disease | 41 |
| Hydrocephaly as sole disease | 2 |
| " with other disease | 8 |
| Microcephaly | 29 |
| Oxycephaly | 1 |
| Plagiocephaly | 3 |
| *Tuberose sclerosis* | 1 |

"organic" group of 138, mongols included, and the "residual" group of 16.

## The Survey

### GENERAL FEATURES OF THE SERIES

When first admitted, only 5 of the 154 children were over 6¼ years of age, and these were all in the "organic" group, 2 being transfers from another institution. The mean age was 35 months (S.D. 19·7) and the range 6–93 months for the "organic" group, and the mean age 50·25 months and the range 22–73 months for the "residual" group, any difference reflecting the prompter recognition of mental defect in physically crippled children. Males were a majority in both groups: 77 (55·8%) in the "organic," and 11 (68·8%) in the "residual" group.

Intelligence was mostly measured by the developmental quotient (D.Q.) on the Vineland scale, but for the present purpose D.Q.'s and I.Q.'s are treated as equivalent. The mean I.Q. of the "organic" group was 23·8 (S.D. 15·6). Though the mean of 39·7 for the "residuals" is not significantly different, there was a very significant excess among them of children with an I.Q. of 31 or more ($P = 0·001$). To exclude any possibility that the findings in this survey simply depended on this I.Q. difference, every result was confirmed by repeating the comparisons with the "residual" group, using a series of cases selected from the "organic" group to match in I.Q., sex, and age.

### COMPARABILITY OF THE TWO GROUPS

If disordered environments are in excess in the "residual" group, it would be mistaken to decide the significance this might have without first ensuring that (1) the hereditary sources of mental defect are equal in both "organic" and "residual" cases; (2) prenatal and obstetric trauma do not explain the "residual" group; and (3) differences do not arise simply from disparity in economic circumstances or in family size.

The following data show that in fact comparison of the two groups is valid.

TABLE II—FAMILIAL FACTORS

| — | "Organic" group (138 cases) | "Residual" group (16 cases) | Significance of difference between groups |
|---|---|---|---|
| *Mother:* | No information in 1 case | | |
| Mentally subnormal | 3·7% (5) | 12·5% (2) | None |
| Epileptic .. .. | 2·3% (3) | 0% (0) | " |
| Total so affected .. | 6% (8) | 12·5% (2) | " |
| *Father:* | No information in 4 cases | | |
| Mentally subnormal | 3% (4) | 0% (0) | None |
| Epileptic .. .. | 0·7% (1) | 0% (0) | " |
| Total so affected .. | 3·7% (5) | 0% (0) | " |
| *Siblings:* | Of 106 with siblings | Of 13 with siblings | |
| Mentally subnormal | 5·9% (6) | 11·5% (1½)* | None |
| Epileptic .. .. | 2·9% (3) | 0% (0) | " |
| Total so affected .. | 8·8% (9) | 11·5% (1½)* | " |
| Dead or stillborn .. | 13·2% (14) | 7·7% (1) | " |
| *Having cousins and/or uncles and/or aunts:* | No information in 2 cases | No information in 1 case | |
| Mentally subnormal | 9·6% (13) | 13·3% (2) | None |
| Epileptic .. .. | 5·9% (8) | 13·3% (2) | " |
| Total with such relative affected .. | 15·5% (21) | 20% (3) | " |
| Parents consanguineous (first cousins) .. | 2·3% (3) | 6·3% (1) | None |
| No consanguinity and no mentally subnormal relative known .. .. | 84·8% (117) | 75% (12) | None |

* Includes 1 case with mentally subnormal half-sibling.

### *Familial Sources of Mental Defect*

Contrary to popular belief, familial factors are seldom prominent when mental defect is as extreme as in these patients. They become so only with milder cases where intelligence lies within the wide range of physiological variation (Penrose 1954). Very few of the relatives of these 154 patients had been certified under the Mental Deficiency Acts. There were only 2 with a parent certified (1 wrongly, as already mentioned), and only 4 with a sibling certified, 1 of these being a "residual" case with a certified half-sibling whose other parent was in a deficiency colony.

Therefore, for the purposes of this survey, the familial sources of mental defect are assessed by combining the handful of relatives statutorily ascertained together with parents and siblings of subnormal mentality conspicuous enough to be recorded in social and clinical reports, and with such cousins, uncles, and aunts specifically stated, by informants in response to routine questioning, to be mentally backward.

Even then it will be seen that defective intelligence is not common in the families of these patients—perhaps no more so than in the general population. Table II shows that the two groups do not differ significantly either in this respect or in the incidence of parental consanguinity, epileptic relatives, and death or stillbirth of siblings, all of which are considered here too because of their occasional association with mental defect.

### *Prenatal, Obstetric, and Neonatal Abnormalities*

Abnormalities of pregnancy, labour, and the neonatal period feature only in the "organic" group.

*Maternal age.*—As expected, this proved to be increased only among mongols. The mean maternal age at birth for the "organic" group, excluding mongols, was 27·5 years (S.D. 7·2), whereas for the "residual" group it was 29 years, and not significantly different. The mean for mongols was 33·7 years, also not very different, but the proportion of their mothers aged more than 40 was 27%, an excess, compared with the other mothers, significant at the 0·1% level.

*Pregnancy.*—With children such as these, the mother's retrospective account of pregnancy probably exaggerates any discomfort and ill health. The information was therefore too subjective for detailed statistical study to be valid. Some degree of objective comparison is made possible, however, by reducing it to show the incidence respectively in the "organic" group, omitting 3 with no information, and the "residual" group of (*a*) threatened miscarriage or bleeding in the first five months—5·2% (7 cases) and 6·3% (1 case); (*b*) pre-eclamptic toxæmia necessitating admission to hospital—11·1% (15 cases) and 6·3% (1 case); and (*c*) other ill health, including specific diseases such as phthisis, undiagnosed symptoms such as alarming gain in weight or in girth, and the statement "felt unwell throughout," but omitting nausea, vomiting, and intercurrent upper respiratory infections—19·3% (26 cases) and 12·5% (2 cases). There is no significant difference in the frequency of these abnormalities, and the figures supply no evidence for placing the ætiology of the "residual" cases in the prenatal environment.

*Obstetric abnormalities.*—The data indicate that neither birth injury nor any sequel apparent in the neonatal period can account for the "residual" cases. A comparison of the obstetric factors in the "organic" group of 98 cases (after excluding mongols because they certainly do not result from birth injury) with the "residual" group shows no statistically significant difference in the respective incidence of (*a*) primogeniture—35% (34 cases) and 56% (9 cases); (*b*) twin birth—5·1% (5 cases) and 6·3% (1 case: the other twin incidentally received different rearing and is not backward; the parents have obstructed every attempt to find out whether they are identical); and (*c*) other obstetric abnormalities—23·5% (23 cases made up of 6 with difficult, prolonged, but spontaneous delivery, 5 with forceps delivery without malpresentation, 7 with malpresentation or breech birth, and 5 with cæsarean section) and 0%.

*Neonatal abnormalities.*—An alarming neonatal condition was significantly commoner in the "organic" group. In it and the "residual" group respectively the neonatal condition (*a*) caused brief anxiety—7·1% (7 cases) and 6·3% (1 doubtful case); (*b*) caused anxiety and the infant to be detained in

hospital more than two weeks, though without special treatment—5·1% (5 cases) and 6·3% (1 case, premature weighing 4½ lb.); or (c) required special treatment—36·7% (36 cases) and 0%. In sum, 49% of the "organic" group presented neonatal abnormalities, in contrast to a doubtful 12·5% in the "residuals"—an excess significant at the 1% level. Nevertheless by the time they left hospital there seems to have been no suspicion of any permanent abnormality in well over half these unsatisfactory neonates, which is a curious finding.

*Family Size* [2]

If 5 "socially illegitimate" cases are omitted, the mean number of children in the families of the "organic" group was 2·3 (S.D. 0·49) if mongols were excluded, and 2·35 including them. It was also 2·3 in the "residual" group, 2 "socially illegitimate" children being likewise omitted. Thus family size does not differ in the two groups.

*Economic Level*

Table III indicates the similarity of the two groups in economic level. Further to exclude any influence of economic factors, every finding mentioned in this survey was confirmed by repeating the comparisons with the "residual" group, using a series of matched cases

TABLE III—ECONOMIC BACKGROUND

| Father's occupation | "Organic" group (138 cases) | "Residual" group (16 cases) |
|---|---|---|
| Managerial and professional | 10% (14) | 12·5% (2) |
| Non-manual wage-earner | 14·5% (22) | 16·8% (3) |
| Manual skilled | 32% (38) | 18·8% (3) |
| Manual semi-skilled and unskilled | 38·8% (58) | 37·5% (6) |
| "Socially illegitimate" | 4% (5) | 12·5% (2) |
| Unknown | 0·75% (1) | 0 |

selected from the "organic" group to coincide in father's occupation and in illegitimacy.

## Rearing and Environment

Statistics are a poor medium for tragedy. This much must be said before proceeding with numerical comparisons for which uneventful lives and individual catastrophes have had to be desiccated alike into uniform factors. The findings given below support the present hypothesis but do not convey the quality of misfortune that beset the "residual" cases so strikingly.

### ADVERSE REARING

The infant's experience consists mainly in the people who rear him and through whom the larger social environment is transmitted—a rôle principally the mother's. With this consideration, it is reasonable to compare the frequency of harmful experiences and upbringing during infancy by assessing the occurrence in each group of "pathological mothering" and "pathological fathering." As expected, the latter did not prove to be important, at any rate directly.

*Pathological Mothering*

This covers experience during the first two years of life of two kinds of disordered mothering—"qualitative" and "quantitative."

In the former, the mother or mother-substitute is severely abnormal psychologically,[3] either overtly psychotic, or known to local social agencies as notoriously

2. For this study, the term "socially illegitimate" distinguishes children born and bred out of wedlock from those illegitimate merely by law, whose parents, while not legally married, in fact kept a house as man and wife and together reared the child.

3. Obviously this category does not include cases where the mother was mentally ill and did not rear the infant. The emphasis here is on the quality of mothering actually experienced and not on the mental health of the mother apart from this.

TABLE IV—PATHOLOGICAL MOTHERING

| Pathological mothering | "Organic" group (138 cases) | "Residual" group (16 cases) | Significance of difference between the groups |
|---|---|---|---|
| Qualitative only | 0% (0) | 25% (4) | + at 0·1% level |
| Quantitative only | 1·5% (2) | 18·8% (3) | + at 0·5% level |
| Both qualitative and quantitative | 3% (4) | 36·3% (5) | + at 0·1% level |
| Total | 4·5% (6) | 75% (12) | + + + at > 0·1% level |

psychopathic, or a feckless dullard so neglectful as to attract the attention of the National Society for the Prevention of Cruelty to Children.

In "quantitative" pathological mothering the infant is without a mother or a definite mother-substitute [4] for an unduly long time; the emotional harmfulness of this is already well substantiated (Bowlby 1951). For such deprivation to be included here, the period, whether continuous or intermittent, must have exceeded an arbitrary minimum of five months in the first year or eight months in the second; and it must not have occurred as a consequence of detection of the child's backwardness. Thus periods away in hospital specifically for investigation of backwardness were disregarded, as also were 3 instances where, at birth, the infant's abnormality was so gross that the mother never had the child at home. Of the cases in the "residual" group listed in table IV as having suffered such deprivation, in only a single example was any part of the period in question simply time in hospital with some serious illness; here it was gastro-enteritis. Every other instance was an outcome of the mismanagement and social chaos surrounding the infant.

Table IV shows the remarkable significance of pathological mothering in the "residual" group. The probability is actually millions to one against its total preponderance being a chance occurrence. The difference in the qualitative category is really reduced because it was

TABLE V—PATHOLOGICAL FATHERING

| Pathological fathering | "Organic" group (138 cases) | "Residual" group (16 cases) | Significance of difference between the groups |
|---|---|---|---|
| Qualitative only | 2·2% (3) | 6·3% (1) | None |
| Quantitative only | 4·4% (6) | 37·5% (6) | + at 0·1% level |
| Both qualitative and quantitative | 2·2% (3) | 12·5% (2) | None |
| Total | 8·8% (12) | 56·3% (9) | + + + at > 0·1% level |

restricted to mothers of the extremely disturbed types specified. Maternal psychoneurosis was disregarded not because its harmfulness to the infant is discounted, but because neuroses are too common, vague, and unequal to be precisely computed here, and because the burden of a defective child mobilises neurotic tendencies. Some information about florid maternal neurosis appears below.

4. There was no instance of a father acting as a consistent mother-substitute—i.e., here "pathological mothering" refers only to a female influence or lack of one. Of the "organic" cases 4 children were reared by a mother-substitute, 2 of these being fostered out when recognised to be mongols, at birth and at 6 months. All the mother-substitutes seemed to provide good care, one being the grandmother, and another so distressed by the child's admission that she soon took him home again. Of the "residual" cases 3 children were reared by a consistent mother-substitute for a while: 2 were with grandmothers for a time, one of whom was a gaol-bird who neglected, and was often separated from, the child; the third child was not reared by the mother at all but, after a time with a foster-mother, was shifted from nursery to nursery.

TABLE VI—DEPENDENCE OF PATHOLOGICAL FATHERING ON PATHOLOGICAL MOTHERING

| — | "Organic" group (138 cases) | "Residual" group (16 cases) | Significance of difference between the groups |
|---|---|---|---|
| Pathologically fathered but not pathologically mothered | 6·5% (9) | 6·3% (1) | None |
| Pathologically mothered but not pathologically fathered | 4·3% (6) | 25% (4) | + at 1% level |
| | (6 cases) | (12 cases) | Significance as given in 2 × 2 contingency tables |
| Prevalence of pathological fathering in cases pathologically mothered | 50% (3) | 56% (8) | None |
| | (12 cases) | (9 cases) | |
| Prevalence of pathological mothering in cases pathologically fathered | 25% (3) | 89% (8) | + at 2·5% level |

*Pathological Fathering*

This is assessed in table v by the criteria used for pathological mothering. Though it is very much commoner in the "residual" group, the significance of this is greatly diminished by the finding (presented in table VI) that, when analysed, the difference in fathering between the two groups depends on the difference in mothering. This is partly because separation from the mother usually involves separation from the father too, and presumably also because pathological mothers tend to mate with unstable men.

*Pathological Rearing*

The disparity between the two groups is summarised in table VII by combining noxious social experiences, both "mothering" and "fathering." Startling as this is, it still conceals by conversion to numbers the depth of adversity suffered by the "residual" patients.

ADVERSE BACKGROUND

Unfavourable factors in the general background again occur to excess in the "residual" group.

*Illegitimacy*

With 31·3% (5 cases) illegitimate, compared with 4·3% (6 cases) of the "organic" group, this was significantly commoner in the "residual" group but only because of the number born to parents living together though not legally married. Thus if such children are distinguished from those "socially illegitimate" as well as legally, illegitimacy in the "organic" and "residual" groups respectively was (*a*) merely legal in 0·7% (1 case) and 18·8% (3 cases), the excess in the "residuals" being significant at the 0·1% level; and (*b*) both legal and social in 3·6% (5 cases) and 13·5% (2 cases), this difference being statistically insignificant.

*Discordant Parents*

Many marriages become strained by a defective child. However, overt marital conflict was significantly commoner among the parents of "residual" patients before the child came on the scene as well as after. Among cases whose parents were living as man and wife there was overt conflict or separation (*a*) in existence before the child's birth in 28·6% (4 cases) of the "residual" group compared with 5·2% (7 cases) of the "organic," an excess significant at the 2·5% level; and (*b*) arising after the child's arrival in 42·9% (6 cases) of the "residual" group and 9% (12 cases) of the "organic," an excess significant at the 0·5% level.

TABLE VII—PATHOLOGICAL REARING

| — | "Organic" group (138 cases) | "Residual" group (16 cases) | Significance of difference between the groups |
|---|---|---|---|
| Pathological rearing, either mothering, or fathering, or both | 13% (18) | 81·3% (13) | +++ at > 0·1% level |

*Psychologically Unhealthy Families* [5]

*Parents.*—Table VIII compares the parents for manifestations of mental disturbance and social inadequacy (mental subnormality has already been considered in table II). This allows further comparison of the emotional background of the two groups, since nearly all the parents took some part in rearing the children, the exceptions in the "residual" cases being 1 mother and 2 fathers (none in the psychologically abnormal categories listed in table VIII) and a like proportion, 8 mothers and 10 fathers, in the "organic" group. Again it is clear that the difference between the groups is far more significant where mothers are concerned; of interest too is the fact that the "residual" cases are most often hampered by mothers with psychopathic personality.

*Siblings.*—There is, unfortunately, insufficient evidence for how siblings fare in the "residual" group. Only 13 patients in this group have siblings, some not reared in the same circumstances. As 9 children are firstborn, most siblings are too young still for unequivocal disorders that could be assessed here. So far, besides the 2 with a sibling or half-sibling mentally subnormal (table II), 2 have siblings known to be child-guidance cases, and 2 have siblings probably as disturbed but not receiving treatment—i.e., nearly half the sibships are abnormal, which is far in excess of the "organic" group, where the proportion is 10% at the outside.

TABLE VIII—MENTAL DISTURBANCE AND SOCIAL INADEQUACY IN PARENTS

| Psychological abnormality | "Organic" group (138 cases) | "Residual" group (16 cases) | Significance of difference between the groups |
|---|---|---|---|
| *Mothers:* | | | |
| Feckless dullards pursued by N.S.P.C.C. | 0% (0) | 12·5% (2) | None |
| Psychosis | 1·4% (2) | 12·5% (2) | None |
| Neurosis, severe enough to need specialist treatment or to be florid before birth of the defective child—i.e., not simply the result of burden of patient | 5·1% (7) | 18·8% (3) | None |
| Gross psychopathy | 1·4% (2) | 31·3% (5) | + at 0·1% level |
| Total | 7·9% (11) | 75% (12) | +++ at > 0·1% level |
| Police convictions: | | | |
| Neglect | 0% (0) | 12·5% (2) | .. |
| Other | 0·7% (1) | 18·8% (3) | .. |
| Total | 0·7% (1) | 31·3% (5) | + at 0·1% level |
| Psychiatric treatment at some time | 4·4% (6) | 43·8% (7) | + at 0·1% level |
| *Fathers:* | Information for 134 only | | |
| Feckless dullards | 0·7% (1) | 0% (0) | None |
| Psychosis | 2·2% (3) | 6·3% (1) | None |
| Severe neurosis as defined above | 1·5% (2) | 6·3% (1) | None |
| Gross psychopathy | 1·5% (2) | 12·5% (2) | None |
| Total | 5·9% (8) | 25% (4) | + at 2·5% level |
| Police convictions | 1·5% (2) | 6·3% (1) | None |
| Psychiatric treatment at some time | 4·4% (6) | 12·5% (2) | None |

5. The reader tempted to see a genetic ætiology for the "residual" cases in the miscellany of psychological disorders prevalent in their families is referred to the discussion of this below.

TABLE IX—CERTAIN DEVELOPMENTAL DETAILS

| — | "Organic" group (matched for age, I.Q., and sex) (16 cases) | "Residual" group (16 cases) | Significance of difference between the groups as given in 2 × 2 contingency tables |
|---|---|---|---|
| Backwardness apparent in first year | Mongols excluded 8 | 1 | + at 2·5% level |
| Unable to walk at 3 years | 4 | 1 | None |
| No control of rectal sphincter at 5 years .. .. | 7 20 cases with defect unrecognised in 1st year | 0 * | + at 1% level |
| History of regression after age of 1 year or more .. | 4 (20%) | 2 (12·5%) | None |

* Some occasionally incontinent but having intervals indicating real ability to control.

*Other relatives.*—The family histories bear out the expectation that the unhealthy parentage of the "residual" cases is the product of diseased backgrounds. Compared with the "organic" group, the "residual" has a greater incidence of mental-hospital treatment, suicide, alcoholism, and crime in one or more of (*a*) the grandparents—40% (6 of 15 cases with available details) against 6% (8 of 136 cases), and (*b*) the uncles, aunts, and cousins—33·3% (5 cases) against 4·5% (6 cases). Both of these excesses are significant at the 0·5% level.

CONCLUSIONS OF STUDY OF REARING AND BACKGROUND

Harmful social influences are overwhelmingly concentrated here among cases of advanced mental defect not attributable to organic disease. So much is evident from statistical analysis, though this omits not only all refined assessment of the infant's early relationships but even the lurid nature of many misfortunes. The total picture is incomplete without mentioning this or remarking that subtler criteria might have accounted for 2 of the 3 "residual" cases not classified in table VII as "pathologically reared."

Obviously a more elaborate study by a team is required with a greater number of "residual" cases, but meanwhile my hypothesis that severe mental arrest sometimes results from severe psychological injury appears reasonably supported. Nevertheless the following alternative explanations of the data must be considered:

(1) *That the "residual" cases are peculiarly selected—i.e., that when lacking organic abnormality, children with mental defect as severe as in these cases are not usually admitted to institutions unless the home is a bad one.*—If this were so, the "residual" cases would probably be admitted earlier than "organics," and here the opposite was the case. Actually, not all severe defectives, "organic" or "residual," enter hospital, and there is nothing to indicate that those who do are simply ones with inferior homes. On the contrary, the facts presented reveal that the great majority come from average homes, and this is as true for those "organic" cases with superficially normal appearance and docile behaviour as for mongols, whose facies alone might make their families get rid of them. The usual difficulty of proving a negative arises if it is to be demonstrated that the "residual" patients in this series are not an unrepresentative sample of such cases in the general population. Though this can only be settled by a mass survey of severe mental defect in the whole child population, it is certain that here, at least, there is no evidence whatever that the "residual" cases are so much more unrepresentative than the "organic" ones that the large differences discovered between them may be dismissed as ætiologically unimportant.

(2) *That the "residual" cases are really examples of as yet unidentifiable organic disorders.*—Of course, it is impossible to prove that some may not be; but, if they all are, their extraordinary association with disturbed environments provides a coincidence which is truly incredible.

(3) *That the "residual" cases have a genetic cause.*—This hypothesis has already had some attention because it was shown above (table II) that mental subnormality and related conditions are not conspicuous in their families; in fact, a third of the parents may even have been of superior intelligence. An assortment of neurotic, psychotic, and criminal deviants is prominent among the forebears, but no hereditary relationship is known between mental disturbance in general and mental defect; nor is one likely. Such an interpretation of the data would be entirely out of touch with modern genetical concepts of heredity on specific mendelian lines (Penrose 1933). Further, the peculiar concentration of mental ill health in the mothers defies simple genetic explanation.

Despite the present findings and others cited, the rôle of emotional injury in the production of mental defect may still be disputed since not *all* infants exposed to harmful social experience become imbeciles. In reply one can only point out that sceptics who reject psychological causes of disease do not rush forward to question the pathogenicity of the tubercle bacillus, though the vast majority infected with it are not ill. As with every pathogen, the outcome, whether minor psychological scarring or major deformity, must depend on the time, the intensity, and the conditions of general health and constitution in which it was operating. Some cases of defect seem to follow psychological trauma that appears not to be gravely destructive, and no doubt they must be explained by some exceptional susceptibility, a subject beyond the scope of this work; its elucidation perhaps may come through direct observation of nursing infants and their mothers, and through concepts such as the "congenital activity types" of Fries (1953).

## Development and Behaviour of the Two Groups Compared

It remains to examine whether psychological injury has distorted the mental development of these children as well as arrested it. Owing to the difference in intelligence levels mentioned above, for valid comparison of developmental and behaviour patterns the "residual" cases were matched against "organic" cases selected to correspond in I.Q., age, and sex.

*Development*

In both groups backwardness was first revealed by slowness of development in the first three years and seldom by regression from some previously attained level; but it became obvious later in the "residual" cases. This difference was significant (table IX), even when mongols were excluded from the comparison because their physical appearance would lead to early diagnosis. Perhaps this is because certain abilities—e.g., erect posture, binocular vision, and primitive sphincter control—are relatively more dependent on the rapid organic maturation of the brain during infancy and so less accessible to psychological disruption. With organic defect there might be general retardation, whereas with

TABLE X—BEHAVIOUR DISORDERS

| Behaviour disorder | "Organic" group (matched for age, I.Q., and sex) (16 cases) | "Residual" group (16 cases) | Significance of difference between the groups as given in 2 × 2 contingency tables |
|---|---|---|---|
| *Socially intolerable and:* | | | |
| Reported before admission .. .. .. | 25% (4) | 86·5% (14) | + at 0·1% level |
| Observed after .. .. | 18·8% (3) | 62·5% (10) | + at 5% level |
| *Externally directed:* | | | |
| Interfering, aggressive, or with destructive outbursts .. .. | 25% (4) | 43·8% (7) | None |
| Prolonged screaming .. | 12·5% (2) | 37·5% (6) | None |
| Smearing fæces .. .. | 0% (0) | 12·5% (2) | None |
| *Not externally directed:* | | | |
| Isolated, self-absorbed, "pseudo-deaf" .. | 6·3% (1) | 50% (8) | + at 2·5% level |
| Repetitious, manneristic | 0% (0) | 37·5% (6) | + at 5% level |
| Self-injuring .. .. | 0% (0) | 43·8% (7) | + at 1% level |

psychogenic defect these may be to some extent spared. The information about acquired abilities was not reliable enough for more detailed comparison than is presented in table IX.

The scatter of intelligence is quite dissimilar in the groups. The total "organic" group, reflecting its multiple ætiologies, is almost evenly distributed at all levels from 0 to 50; the "residual" cases, in contrast, are clustered round the mean of 39·7 (S.D. 5·9), and this further supports some homogeneous ætiology.

*Distorted Behaviour*

The "residual" group presents behaviour disorder both more commonly and in peculiar forms. The disparity is indicated in table X, which only lists disturbance that was socially intolerable. It discloses that, though externally directed behaviour disorder, such as destructiveness and screaming, occurred in both groups, activity with no external direction, such as repetitious, self-absorbed, and self-injuring types, was practically confined to the "residual" cases; some children, at times, were so withdrawn as to be suspected of deafness.

## Clinical Picture of Psychogenic Defectiveness

The outlines of the condition isolated now emerge. The young child, though physically healthy, will present severe backwardness evident from about the second year, with curious behaviour disorder and a history of perverted mothering in infancy. In his first two years he will either have been reared by an extremely disordered person, commonly a psychopath, or else deprived for long and repeated periods of the mother or her substitute; usually he will have suffered both misfortunes. None here were simply reared in an institutional setting—of 3 so reared from the age of 18 months or less 2 first endured terrible neglect by unstable mothers, 1 passing later through five institutions, while the 3rd went from foster-mother to institution to institution.

Clinically these children's backwardness is uneven; despite an I.Q. about 40, their early milestones are not much delayed, and they lack the clumsiness and impoverished expression of other imbeciles—some, indeed, are very graceful and attractive. At times they appear extraordinarily remote and even deaf, tending to monotonous mannerisms, banging their heads, and tearing their hair out; many also have intolerable propensities for screaming and destructiveness.

Of those I have observed in hospital for a year or two beyond their 5th birthday, some become docile imbeciles, and others burnt out and dilapidated ones; yet others do not change.

## Practical Importance of Psychogenic Defect

The condition described here must be of great social interest since it cannot be rare, it is probably preventable, and it may initially be treatable.

*A Common Condition*

At the Fountain Hospital about 10% of severe aments seem to be in this category. Admissions are from a big area and without any special selection, and this figure must be fairly representative of extreme defectives under hospital care. The condition may therefore be responsible for many thousands of people occupying hospital beds in this country. Moreover, this is a restricted estimate confined to psychogenic defect in apparently pure culture. The condition may be even commoner for the following reasons:

(1) Milder emotional undernourishment or damage, or an equal degree in a more resistant victim, may account for some of the less extreme defectives in the community, and even more of those in institutions (Hilliard and Mundy 1954).

(2) Some mental defectives of organic ætiology may have been reduced to the institutional level by such trauma, additionally. Possibly these children are less equipped to overcome indifferent rearing and very liable, by virtue of physical deformity, to elicit it.

*A Preventable Condition*

The histories of these cases monotonously disclose how little realisation still exists among social agencies, doctors, and hospitals that a small infant is a social being who needs more than food alone to grow up. For example, the digestive difficulties, failure to thrive, and napkin rashes common in these infants, and a crying illustration of maternal incompetence, led to their spending weeks at a time in hospital, always to be discharged "recovered," and always to relapse with another complaint, but never led to serious probing of the mother. Even when backwardness was obvious, the exclusion, often recondite, of physical disease left inquiry exhausted; in all 5 cases in this series where the child was under one hospital while the mother was under another for psychological treatment no communication appears ever to have passed between the two.

*A Treatable Condition*

These conditions are man-made. If recognised early and given therapeutic environments, with sensitively skilled nursing and intensive psychotherapy, they are possibly reversible; there is every indication of this in the therapeutic work of Rank (1949), in Boston, with "atypical" children, and of David and Appel (1951), in Paris, with *arriération psychogène*. No such facilities are enjoyed at the Fountain Hospital.

## Protophrenia: Theoretical Significance of Psychogenic Defect

Its theoretical significance will need elaboration elsewhere, but it will be mentioned here that the condition has bearings on the nosology of mental disorder in childhood, on ego psychopathology, and on the psychology of intelligence.

*Nosology of Mental Disorder in Childhood*

It will have become apparent that these children may superficially resemble adults with chronic schizophrenia. However, similar behaviour does not mean identical psychopathology, and merely to label these defectives as psychotic deprives the term of any precise meaning. Generally, psychosis designates disorders where ego functions disintegrate, where the person ceases to be himself. These children have no such disorder, and far from presenting disintegration, with 2 exceptions, they achieved integration at no time at all, their disruption being presumably of primitive infantile processes assembling towards an organised personality. The early distortion of those unintegrated processes that survive may account for the curious behaviour which characterises these patients.

Protophrenia seems to me a suitable name for this condition, implying an aborted organisation of the personality as distinct from disorganisation, to which psychosis refers, and from undistorted retardation accompanying organic cerebral defect, which, by itself, seldom produces autistic behaviour disorder, to judge from the material here.

It is uncertain how protophrenia is related to the syndrome of "early infantile autism" (Kanner 1944). There seem to be differences in that a proportion of the cases here are not autistic and in that only some of Kanner's cases were regarded as mentally defective and none are described as having behaviour disturbances apart from lack of emotional relationship to people and monotonous adherence to some daily routine. The background of his cases was different too, containing an excess of socially and intellectually superior forebears.

*Psychopathology of Ego Functions*

Protophrenia can be regarded as a psychogenic failure of ego formation. Its study must be relevant to that of pathological ego formation, generally, where early

emotional trauma is at all important. This includes the fragility underlying adult schizophrenia and child psychoses, and the maldevelopment of psychopathic adults and problem children. The present arrangement whereby mental deficiency, child guidance, and adult psychiatry are practised in almost complete isolation from one another can only impede understanding of the common processes basic to each.

*Psychology of Intelligence and Mental Defect*

The fact that extreme mental defect can be related to unfavourable rearing promotes the view that lesser deviations of mental ability are highly susceptible to nurture and are not simply a matter of genes. The relevance of this to mental defect of organic ætiology has already been mentioned; mental hygiene rather than eugenic programmes may be the way to alleviate the social problem of mental defect and to promote intelligence.

## Summary

This work indicates that extreme mental defect may be attributable to grossly perverted infant rearing in about 10% of cases. This group alone may be occupying thousands of hospital beds and in frequency may be second only to mongolism as a type of severe amentia.

For many years attention has been devoted to psychological injury in early life as a cause of mental disorder, but the same possibility has been almost ignored in severe mental defect, because this is usually associated with obvious organic disease. The possibility is evident from classical studies of institutional infants, from a measure of success in psychotherapy with imbecile children, and from experiments on animals.

An objective survey was devised to discover whether emotionally unfavourable environments are significantly commoner among severe cases of mental defect with no discernible organic cause. A consecutive series of 154 child cases was separated clinically into "organic" (138) and "residual" (16) groups. The experiences and background of each were tabulated and compared statistically, the information obtained being independent of any subjective bias of the examiner. A remarkable preponderance of destructive social influences was demonstrated in the "residual" cases, and no explanation can displace their ætiological importance.

A clinical picture of psychogenic amentia is drawn, and it was also shown statistically that certain patterns of development and distortions of behaviour are characteristic.

The condition is of considerable social importance. Similar causation may account for many cases of mental defect milder than those described here, and in cases with brain damage environmental factors may aggravate the defect to such an extent that the child requires institutional care.

Its nosology is discussed; it appears to be an abortive failure in organisation and integration of ego functions. Protophrenia is the name suggested to distinguish this from psychosis, in which ego organisation forms and then disintegrates, and from organic retardation, which has a different clinical picture lacking certain patterns of development and behaviour disturbance. The understanding of ego psychopathology is impeded by the unnatural divorce of mental deficiency from other branches of psychiatry; for there are pathogenic processes common to all.

Psychogenic defect is man-made and preventable, and perhaps cases detected early may be reclaimed. A plea is made for seeking to alleviate the social burden of mental defect and to promote intelligence by mental hygiene rather than by eugenic programmes.

I am deeply indebted to Mr. Frank Orford, M.A., of University College, London, for sharing the labour of some 400 statistical calculations and for many stimulating ideas. Likewise, I thank the records-office staff at the Fountain Hospital for unstinted and unpaid assistance with the great mass of documentation. I am grateful to Dr. L. T. Hilliard, Dr. Brian Kirman, and my colleagues for encouragement and facilities for the work, given most generously.

### REFERENCES

Bowlby, J. (1951) Maternal Care and Mental Health. London.
Burt, C. (1947) Mental and Scholastic Tests. London.
Crome, L. (1954) *J. ment. Sci.* **100**, 894.
David, M., Appel, G. (1951) *Rev. Psychiat. infant.* **18**, 205.
Fries, M. (1953) *Psychoanal. Study Child*, **8**, 48.
Goldfarb, W. (1945) *Amer. J. Psychiat.* **102**, 18.
Hilliard, L. T., Mundy, L. (1954) *Lancet*, ii, 644.
Hollingshead, A. B., Redlich, F. C. (1954) *Amer. J. Psychiat.* **110**, 695.
Kanner, L. (1944) *J. pediat.* **25**, 211.
Klein, M. (1932) The Psycho-Analysis of Children. London.
Lorenz, K. (1935) *J. Ornith.* **83**, 137.
Pearson, E. S., Hartley, H.O. (1954) Biometric Tables for Statisticians. Cambridge.
Penrose, L. S. (1933) Mental Defect. London.
— (1938) *Spec. Rep. Ser. med. Res. Coun., Lond.* no. 229.
— (1954) The Biology of Mental Defect. London.
Promptov cited by Popovsky (1953) Vremmenie Svyazi. Moscow.
Rank, B. (1949) *Amer. J. Orthopsychiat.* **19**, 130.
Spitz, R. A. (1945) *Psychoanal. Study Child*, **1**, 53.
— (1946) *Ibid*, **2**, 113.
Wahl, C. W. (1954) *Amer. J. Psychiat.* **110**, 668.

# ROSEOLA INFANTUM

## A REVIEW OF FIFTY CASES

A. LETCHNER
M.D. Berlin, L.R.C.P.E.
HONORARY PHYSICIAN, HARROW HOSPITAL

ROSEOLA infantum was first described and named by Zahorsky (1910) in the U.S.A. Others have called it exanthema subitum, exanthema criticum, three-day fever, and sixth disease. Many reports on it have been published in the U.S.A., and a smaller number of papers have appeared in many European and overseas countries. According to Berenberg et al. (1949) it is probably the most common febrile exanthem in children aged less than 3 years in the U.S.A. Only very few papers about it have been published in this country.

The fact that I have observed 50 cases in general practice between 1943, when I first became acquainted with it, and 1955 shows that roseola infantum is also quite common in this country. The cases were fairly evenly spread over the twelve years and were all sporadic so far as I could ascertain.

The following are the main characteristics of roseola infantum:

(1) It occurs nearly exclusively in the first three years of life.

(2) There is an initial febrile stage with fairly high pyrexia and very little to account for it. It lasts several days, most commonly three.

(3) Rather surprisingly—hence the name exanthema subitum—when the temperature is settling or has settled down, and the child is getting well, a rash like rubella or very mild measles appears and the illness ends.

(4) Complications scarcely ever arise. No fatal case has been described.

(5) Roseola infantum practically always confers permanent immunity to it.

The great majority of cases reported have been sporadic, but there have been some contact cases, and descriptions of small epidemics, mainly in homes for babies, have been published.

Kempe et al. (1950) transmitted roseola infantum from a child in the pre-eruptive stage to a baby kept in isolation; the baby developed the typical disease after nine days. Clinical experience appears to fix the incubation period at eight to fifteen days (Cushing 1927, Greenthal 1922, Berenberg et al. 1949).

All attempts to isolate the causal organism, probably a virus, have so far been unsuccessful.

### Incidence

My 2 youngest patients with roseola infantum were both aged 3½ months, and I had 3 aged more than 3 years. The age-distribution of my cases was as follows:

| Age (mos.) | No. of cases |
|---|---|
| Up to 6 | 5 |
| 6–12 | 12 |
| 13–18 | 16 |
| 19–24 | 9 |
| 25–30 | 1 |
| 31–36 | 4 |
| 40 | 1 |
| 50 | 1 |
| 63 | 1 |

In other words 66% of cases occurred in the first 18 months of life, 84% in the first 2 years, 94% in the first 3 years, and 6% later.

Up to 1947—according to Zahorsky (1948)—less than a score of cases had been reported in children over 4 years of age.

It is generally agreed that the sexes are about equally affected; of my patients 26 were male and 24 female.

According to Zahorsky (1940) in 300 cases the disease was most prevalent during autumn and spring. My cases were fairly evenly spread throughout the year: 5 in January, 5 in February, 4 in March, 5 in April, 5 in May, 3 in June, 4 in July, 1 in August, 4 in September, 7 in October, 4 in November, and 3 in December.

### Illustrative Case-reports

The following are 2 typical case-reports:

**Case 1.**—A baby, aged 15 months, became irritable on Jan. 13, with loss of appetite, temperature 103·5°F, slight coryza, and injected pharynx. Next day some small swollen occipital glands were detected (temperature still 103·5°F). On Jan. 15 the condition was unchanged and nothing abnormal was detected in ears, chest, or urine. On Jan. 16 the temperature fell to 100·2°F and the general condition improved somewhat. On Jan. 17 the temperature was 99·0°F, the baby was apparently well, and a pink macular rash appeared, which disappeared in forty-eight hours (fig. 1).

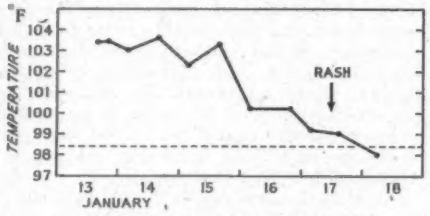



Fig. 1—Relation of pyrexia to rash in case 1.

**Case 2.**—A baby, aged 12 months, became ill on Oct. 3 with slight diarrhœa, restlessness, loss of appetite, temperature 104·0°F, and slightly injected pharynx. Next day the temperature was 101·2°F in the morning and 105·0°F in the evening, but there were no other signs of illness. On Oct. 5 the temperature was 100·6°F in the morning and 103·0°F in the evening. On Oct. 6 the temperature was 99·2°F. On Oct. 7 the temperature was 98·4°F and a rubelliform rash appeared, which disappeared in twenty-four hours (fig. 2).

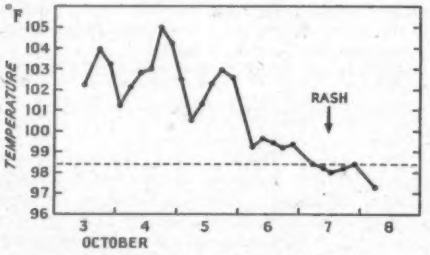



Fig. 2—Relation of pyrexia to rash in case 2.

### Temperature

In 22 of my cases an exact record of the temperature was kept: in 10 of these the maximum was 104–105°F, in 8 102–104°F, and in 4 100–102°F.

15 infants had remittent, 6 continuous, and 1 intermittent pyrexia.

The pyrexia lasted one day in 2 cases, two days in 4, three days in 25, four days in 10, and five days in 1 case. In 8 cases the history was too vague to determine the length of the pyrexia.

According to the published reports the most common duration of the pyrexia is three to five days, but it has lasted as long as nine days.

Zahorsky (1940) saw the majority of his 300 cases end by crisis. Of my 22 cases in which the temperature was recorded 13 ended by crisis and 9 by lysis.

### Symptoms and Signs in Pyrexial Stage

During the pyrexial stage some children appear to have surprisingly little discomfort, in spite of high temperatures, but others are restless, sleepless, do not eat, and appear to be in pain.

There is a characteristic lack of signs in the pyrexial stage: of my 50 cases 7 had a red throat, 4 a mild watery coryza, 4 reddened conjunctivæ, 12 a slight cough, 3 initial vomiting, 3 a few loose stools, 1 follicular tonsillitis, 1 flushed drums, and 1 a mucoid vaginal discharge. All these signs disappeared when the temperature came down and the rash appeared.

The most common sign during the pyrexial period was swollen lymph-glands: these were present in 22 cases (44%); in 16 cases occipital glands were enlarged, in 8 cases posterior cervical, in 3 posterior auricular, and in 1 axillary.

All workers emphasise that the catarrhal signs, if present at all, are generally very mild; only few cases with follicular tonsillitis and very few with suppurative otitis media have been described.

The occasional appearance of a distinct enanthema on soft palate or uvula has been noted by Glanzmann (1934) and by Berenberg et al. (1949).

In a varying proportion of cases—the reported incidence in different series varies between 0·7% and 50%—convulsions have been observed during the pyrexial stage; no convulsions occurred in my cases.

The white-cell count shows nearly always, at least after the first twenty-four to thirty-six hours, a definite leucopenia with relative lymphocytosis.

I made a white-cell count in 3 of my cases: the leucocytes numbered 5000 per c.mm. (lymphocytes 40%), 4600 per c.mm. (lymphocytes 44%), and 2400 per c.mm. (lymphocytes 80%).

The appearance of the rash coincided generally with the drop in temperature.

In 42 of my cases either the patient had already been seen in the pyrexial stage or the history was sufficiently clear-cut to determine the relationship between temperature and rash; in 32 of them the rash appeared on the day of the temperature drop, in 5 it appeared twenty-four hours later, in 1 thirty-six hours later; in 4 cases it began to appear the day before the temperature went down.

### The Rash

The rash is composed of discrete pink macules, but occasionally it is slightly papular; in my cases it began usually on the trunk, more often on the back than on chest or abdomen; in other cases it appeared first at the nape of the neck, at the forehead-hair border, or behind the ears. When fully developed it usually covered most of the trunk, the nape of the neck, often the upper part of the limbs, and occasionally the scalp. The face was only rarely and then sparsely affected. In a few cases the rash coalesced on part of the back but not so extensively as a typical scarlet-fever rash.

The rash was usually fully developed in twenty-four hours. Its total duration was in most of my cases forty-eight hours, but in some it had already disappeared in twenty-four hours; in a few others it lasted up to seventy-two hours.

It did not appear to itch; it was not followed by desquamation or pigmentation.

Cases of roseola infantum without rash have been seen by other observers during epidemics in homes for babies.

### Immunity

The fact that roseola infantum rarely occurs after the age of 3 years suggests that by that time nearly all children have become immune to it, but, since only a minority of children suffer from a typical attack, it appears that by the age of 3 years many have become immune through a modified illness, either without a rash or with a very sparse or fleeting one. On the other hand Wesselhoeft (1951) suggests that roseola infantum might occur in older children and adults without a rash or with a nocturnal rash only. This would put roseola infantum in the exceptional position of being an exanthematic disease occurring in one age-group usually with a rash and in the rest usually without a rash or with a nocturnal rash only, which seems to me unlikely.

### Diagnosis

In the presence of an otherwise unexplained persistent pyrexia in a child of the most susceptible age-group, possibly with enlarged lymph-glands at the back of head or neck, the diagnosis of roseola infantum should be considered among other causes of pyrexia of unknown origin. A well-marked leucopenia with relative lymphocytosis would support the diagnosis.

Once the rash has appeared, mainly rubella, measles, and drug rashes have to be considered in the differential diagnosis. Though the rash of roseola infantum is very similar to the rash of german measles or very mild measles it does not affect the face or only very slightly.

In roseola infantum catarrhal symptoms are absent or at the most very mild; there are no Koplik's spots.

The most important characteristic of roseola infantum is that the rash appears when the child is beginning to recover, whereas in rubella the pyrexia and the rash coincide, and in measles the rash appears while the illness is reaching its climax.

### Summary

Roseola infantum is a common infective disease, occurring nearly exclusively in the first 3 years of life; 50 cases of it were seen in twelve years of general practice.

Complications are very rare; no fatal cases have been reported.

The treatment is symptomatic.

### BIBLIOGRAPHY

Banks, H. S. (1949) Common Infectious Diseases. London.
Barenberg, L. H., Greenspan, L. (1939) *Amer. J. Dis. Child.* **58**, 983.
Berenberg, W., Wright, S., Janeway, C. A. (1949) *New Engl. J. Med.* **241**, 253.
Breese, B. B. jun. (1941) *N.Y. St. J. med.* **41**, 1854.
*British Medical Journal* (1950) ii, 876.
Clemens, H. H. (1945) *J. Pediat.* **26**, 66.
Conte, A. N., Uzmann, J. W., Ware, G. W. (1944) *Arch. Pediat.* **61**, 559.
Craddock, D. (1953) An Introduction to General Practice, London; p. 480.
— (1955) *Brit. med. J.* i, 1219.
Cushing, H. B. (1927) *Canad. med. Ass. J.* **17**, 905.
Cutts, M. (1938) *Ann. intern. Med.* **11**, 1752.
Dickey, L. B. (1945) *Stanf. med. Bull.* **3**, 37.
Faber, H. K., Dickey, L. B. (1927) *Arch. Pediat.* **44**, 491.
Farber, S. (1938) *New Engl. J. Med.* **219**, 836.
Glanzmann, E. (1924) *Schweiz med. Wschr.* **54**, 589.
— (1934) *In* Handbuch innerer Medizin. Edited by G. von Bergmann and R. Staehelin. 3rd ed., Berlin; vol. I, p. 420.
Greenthal, R. M. (1922) *Amer. J. Dis. Child.* **23**, 63.
Harries, E. H. R., Mitman, M. (1947) Clinical Practice in Infectious Disease. Edinburgh.
Heiman, H. (1925) *Arch. Pediat.* **42**, 447.

*Bibliography continued at foot of next column*

# ANTIBIOTIC THERAPY OF TUBERCULOSIS OF THE FEMALE GENITALIA

I. HALBRECHT
M.D. Strasbourg
*From the Maternity Hospital, Hadera, Israel*

ALMOST five years have elapsed since our first results of streptomycin treatment of 12 cases of latent female genital tuberculosis were published (Halbrecht 1951). We have since treated 62 more cases of tuberculosis of the female genitalia in all its stages and have followed up some of them for more than five years since the start of antibiotic treatment.

Almost all of these patients sought our help not because of genital tuberculosis, of which they were hardly, if at all, aware, but because of sterility. Thus, the assessment of any treatment of female genital tuberculosis must take into account not only its ability to cure the tuberculosis but also its effect on the sterility, which is the main complication of the tuberculosis.

### Diagnosis

It is generally agreed that in the first stages of tuberculosis the fallopian tubes alone are involved, and that endometrial tuberculosis represents a later stage, the tuberculosis spreading slowly but continuously by contact from the endosalpinx to the endometrium (Sutherland 1943, Sharman 1944, Halbrecht 1946, Berblinger 1946, Liljedahl and Ryden 1950, Schockaert 1951).

It is therefore obvious that, in female genital tuberculosis, the earlier the antibiotic treatment is instituted the more likely it is to be successful, especially so far as sterility is concerned. For this reason we tried to diagnose the tuberculosis, which is asymptomatic in more than 90% of cases, by culture of menstrual and intermenstrual discharges. By this method it is possible to diagnose genital tuberculosis in its early, pre-endometrial, stage in a considerable number of cases.

### Material

We treated with streptomycin and *p*-aminosalicylic acid (P.A.S.) 74 cases of female genital tuberculosis, of which 21 were discovered in the tubal stage and 49 in the endometrial stage, and 4 were exudative cases with more or less large tumours in the adnexa (table I).

### Methods

Our first 12 patients were treated by daily injections of streptomycin 1 g. alone. Each of them received 45 g. The 62 other patients received a combined treatment of streptomycin 1 g. thrice a week to a total of 45–50 g. and P.A.S. 12 g. daily to a total of 800–900 g.

---

### DR. LETCHNER: BIBLIOGRAPHY—*continued*

Hynes, M. (1940) *Lancet*, ii, 679.
Jackson, D. C. (1949) *Med. J. Aust.* ii, 52.
James, U., Freier, A. (1949) *Arch. Dis. Childh.* **24**, 54.
Jennings, R. E. (1940) *J. med. Soc. N.J.* **37**, 577.
Kempe, C. H., Shaw, E. B., Jackson, J. R., Silver, H. K. (1950) *J. Pediat.* **37**, 561.
Levy, D. J. (1921) *J. Amer. med. Ass.* **77**, 1785.
McQuitty, E. L. (1955) *Brit. med. J.* i, 1005.
Park, J. H. jun., Michael, J. C. (1922) *Amer. J. Dis. Child.* **23**, 63.
Rosenblum, J. (1945) *Ibid*, **69**, 234.
Ruh, H. O., Garvin, J. A. (1923) *Arch. Pediat.* **40**, 151.
Schlesinger, B. (1937) *Brit. med. J.* i, 298.
Veeder, B. S., Hempelmann, T. C. (1921) *J. Amer. med. Ass.* **77**, 1787.
Wallfield, M. J. (1934) *J. Pediat.* **5**, 800.
Wesselhoeft, C. (1951) *In* Banks, H. S. Modern Practice in Infectious Fevers. London; vol II.
Westcott, T. S. (1921) *Amer. J. med. Sci.* **162**, 367.
Yoshina, T. (1942) *Hawaii med. J.* **1**, 235.
Zahorsky, J. (1910) *Pediat.* **22**, 60.
— (1925) *Arch. Pediat.* **42**, 610.
— (1940) *Ibid*, **57**, 405.
— (1947) *Ibid*, **64**, 579.
— (1948) *In* Brennemann Practice of Pædiatrics. Hagerstown, Md.; vol. II, chapter 21.

TABLE I—CLASSIFICATION OF CASES BY METHOD OF DIAGNOSIS

| Group | Stage | Diagnostic means and results | | No. of cases |
|---|---|---|---|---|
| | | Endometrial biopsy | Culture | |
| I | Tubal | Negative | Positive | 21 |
| II | Endometrial | Positive | Positive | 49 |
| III | Exudative | .. | Positive | 4 |
| Total | .. | .. | .. | 74 |

11 patients in whom this first course of antibiotic treatment was unsuccessful received a second course of treatment consisting of streptomycin 60–75 g. and P.A.S. 1200 g.

In 6 cases the streptomycin was discontinued before 30 g. had been given, because vestibular symptoms appeared.

In cases in which endometrial biopsy had revealed endometrial tuberculosis, biopsy was repeated at six-month intervals after the treatment. In cases in which cultures of menstrual discharges had been positive, cultures were repeated every month during the first year and every two or three months in the years following the treatment.

## Results

Only 68 of the 74 patients received the full treatment of 45 g., which is the minimum needed to cure latent tuberculosis of the female genitalia. Nevertheless I report here the results (table II) obtained in all 74 cases,

TABLE II—RESULTS AND FOLLOW-UP

| Months after treatment | 12 | 13–24 | 25–36 | 37–48 | 49–60 | 61–74 | Total |
|---|---|---|---|---|---|---|---|
| Cures .. .. | 3 | 8 | 11 | 8 | 11 | 7 | 48 |
| Recurrences .. | 10 | 14 | 2 | .. | .. | .. | 26 |

including the 6 in which only about 30 g. of streptomycin was given, because I have been impressed by the lasting successful results in some patients with even this small amount of streptomycin.

In 48 of the 74 patients, treated with streptomycin alone or in combination with P.A.S., no signs of genital tuberculosis could be discovered from one to six years after the treatment.

Of these 48 patients 7 were under continuous observation for more than five years after the treatment, 11 for more than four years, 8 for more than three years, 11 for more than two years, 8 for more than a year, and 3 for a year.

3 of the 6 patients who did not receive more than 30 g. of streptomycin were free from any signs of genital tuberculosis for more than three years, whereas the 3 others showed a recurrence of tuberculosis before the end of the second year after the treatment.

*Endometrial Tuberculosis* (table III)

Tuberculosis recurred in 16 of 49 patients who had endometrial tuberculosis before the treatment. In only 8 of these was the recurrence endometrial; in the other 8 it was tubal, found by positive culture of menstrual and intermenstrual discharges, whereas endometrial biopsy was repeatedly negative after the treatment.

TABLE III—RESULTS OF ANTIBIOTIC TREATMENT IN ENDOMETRIAL TUBERCULOSIS

| Months after treatment | 12 | 13–24 | 25–36 | 37–48 | 49–60 | 61–72 | Total |
|---|---|---|---|---|---|---|---|
| Cultures and endometrial biopsy negative .. | 2 | 3 | 9 | 6 | 8 | 5 | 33 |
| Cultures positive and endometrial biopsy negative .. .. | 5 | 3 | .. | .. | .. | .. | 8 |
| Endometrial biopsy positive .. .. .. | 4 | 3 | 1 | .. | .. | .. | 8 |
| Total positive .. .. | 9 | 6 | 1 | .. | .. | .. | 16 |

In 3 of the 8 cases in which endometrial tuberculosis recurred the first endometrial biopsy after treatment was negative, and only the second, done six months later, showed endometrial tuberculosis. Long before the positive endometrial biopsy, cultures of menstrual discharges were positive for tuberculosis in these 3 cases. It therefore seems that antibiotic treatment is more effective in curing endometrial than tubal tuberculosis.

*Tubal Tuberculosis* (table IV)

The only means of diagnosing female genital tuberculosis in the tubal stage, before involvement of the endometrium, is culture of menstrual and intermenstrual discharges.

In 7 of the 21 cases of isolated tubal tuberculosis positive cultures of the genital discharges showed a recurrence of tuberculosis within two and a half years of the start of the treatment.

TABLE IV—RESULTS OF ANTIBIOTIC TREATMENT IN TUBAL TUBERCULOSIS

| Months after treatment | 12 | 13–24 | 25–36 | 37–48 | 49–60 | 61–72 | Total |
|---|---|---|---|---|---|---|---|
| Negative cultures .. | 1 | 4 | 2 | 4 | 1 | 2 | 14 |
| Positive cultures .. | 2 | 4 | 1 | .. | .. | .. | 7 |

*Exudative Tuberculosis*

In 4 cases bimanual genital examination revealed a tumour of the adnexa which was clinically thought to be tuberculous. The diagnosis was confirmed by positive culture of the menstrual discharges.

Each of these 4 patients received 60–75 g. of streptomycin and 1200 g. of P.A.S. In 2 cases the tumour disappeared completely, and in the 2 others it diminished but did not disappear. In 3 of the 4 cases culture of the menstrual discharges became positive from six to eighteen months after the treatment.

*Effect of Antibiotic Treatment on Sterility caused by Genital Tuberculosis*

7 ectopic and 5 intra-uterine pregnancies followed the antibiotic treatment of genital tuberculosis in the 74 patients. They were distributed as follows:

5 ectopic and 3 intra-uterine pregnancies occurred in 7 patients with isolated tubal tuberculosis. The 3 intra-uterine pregnancies went to their end, full-term healthy babies being born.

TABLE V—RESULTS OF SECOND COURSE OF ANTIBIOTIC TREATMENT

| Months after treatment | 12 | 13–24 | 25–36 | 37–48 | 49–60 | Total |
|---|---|---|---|---|---|---|
| Cures .. .. .. | .. | 1 | 3 | 1 | 1 | 6 |
| Recurrences .. .. | 5 | .. | .. | .. | .. | 5 |

2 ectopic and 2 intra-uterine pregnancies occurred in 4 patients with endometrial tuberculosis who had been completely cured by the antibiotic treatment. The 2 intra-uterine pregnancies ended in miscarriages in the third and fourth months.

Histological examination of the tubes in the 7 ectopic pregnancies revealed the persistence of tuberculosis in the walls of the tubes in 1 case and no tuberculosis in the others.

Histological examination of curettage material in the 2 cases of miscarriage did not reveal any tuberculosis.

3 ectopic pregnancies occurred immediately after the antibiotic treatment, and the other 4 one or two years after the treatment.

Both full-term pregnancies in the patients with healed tubal tuberculosis and both miscarriages in the patients with healed endometrial tuberculosis occurred in the second year after the treatment.

*Second Course of Treatment* (table v)

11 of the 26 patients in whom the first series of streptomycin injections did not cure the genital tuberculosis received a second course, which consisted of streptomycin 60 g. and P.A.S. 1200 g. In 5 of these patients the tuberculosis recurred within a year from the start of the second course. The 6 other patients are free from tuberculosis from two to four years after the second course, but none of them has yet conceived.

### Discussion

No treatment of female genital tuberculosis can be properly assessed except by comparing its results with the incidence of spontaneous healing of this disease and the occurrence of pregnancies in untreated cases.

Spontaneous healing of female genital tuberculosis is very rare but undoubtedly takes place. In 6 of 90 cases of untreated endometrial tuberculosis and in 1 case of tubal tuberculosis spontaneous healing could be assumed on the basis of repeated negative endometrial biopsies and a great number of negative cultures of the menstrual discharges made repeatedly during at least from two to five years after the diagnosis of genital tuberculosis had been established by a positive endometrial biopsy or by positive cultures of the genital discharges.

No patient with apparently healed endometrial tuberculosis conceived, whereas the patient with healed tubal tuberculosis conceived and was successfully delivered.

Thus it seems that spontaneous healing of endometrial tuberculosis does not improve the chances of pregnancy in these patients. On the other hand, in cases in which spontaneous healing starts in the earliest, or tubal, stage, when functional restitutio ad integrum of the tubes is still possible, pregnancy may take place.

### Conclusions

Analysis of the results of antibiotic treatment of female genital tuberculosis leads to the following conclusions:

(1) The combined treatment of female genital tuberculosis with streptomycin 45 g. and P.A.S. 800 g. led to healing of the disease in about 65% of cases.

(2) More than half the patients in whom the first course of antibiotic treatment was ineffective benefited from a second course of streptomycin and P.A.S.

(3) Healing of female genital tuberculosis cannot be considered definite until at least three years have elapsed since the start of treatment.

(4) For this reason all the patients must remain under strict observation, and endometrial biopsies and cultures of the menstrual discharges must be repeated at regular intervals during the first five years after treatment. A second course of streptomycin and P.A.S. should be given as soon as the first signs of recurrence of tuberculosis are discovered, whether on endometrial biopsy or in cultures of the menstrual discharges.

(5) Cultures of the menstrual discharges were much more valuable than endometrial biopsy in discovering recurrence of female genital tuberculosis.

(6) There is no doubt that in some cases antibiotic treatment cured the sterility caused by genital tuberculosis, especially in the tubal stage.

(7) Antibiotic treatment was followed by ectopic pregnancy more often than by intra-uterine pregnancy.

(8) 3 intra-uterine pregnancies after antibiotic treatment went to term in genital tuberculosis healed at the tubal stage, whereas in both cases of healed endometrial tuberculosis pregnancy ended in a miscarriage.

### Summary

In 48 of 74 women with genital tuberculosis treated with streptomycin and P.A.S. the disease did not recur after a first course of antibiotic treatment consisting of streptomycin 45 g. and P.A.S. 800 g. In 6 of 11 women given a second course, which consisted of streptomycin 60 g. and P.A.S. 1200 g. the genital tuberculosis was cured.

7 ectopic and 5 intra-uterine pregnancies occurred in 11 of the patients in whom the genital tuberculosis was cured by antibiotic treatment.

*References at foot of next column*

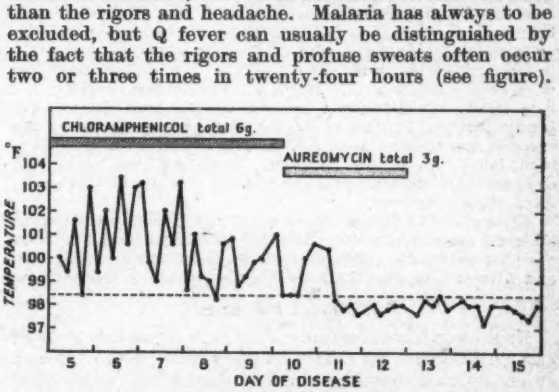
# Q FEVER IN NAKURU, KENYA

A. L. CRADDOCK
O.B.E., M.B. Lond.
GENERAL PRACTITIONER, NAKURU

JAMES GEAR
M.B. Witw'srand, D.P.H., D.T.M. & H., Dip. Bact.
DEPUTY DIRECTOR, SOUTH AFRICAN INSTITUTE FOR MEDICAL RESEARCH, JOHANNESBURG

SOON after arrival in Nakuru three years ago, one of us (A. L. C.) was struck by the frequency of an acute febrile illness with pneumonic features, which was usually regarded as virus pneumonia. It strongly resembled Q fever, and the help of the other (J. H. S. G.) was enlisted to confirm its cause. Tests soon showed that many cases were in fact infections with *Rickettsia burneti*, and there is no doubt that this disease is endemic in the locality. Nakuru itself is a large market town a hundred miles north-west of Nairobi, surrounded by an extensive dairy-farming area occupying the floor and slopes of the Rift Valley. Cattle are a well-recognised source of infection (Harvey et al. 1951, Marmion et al. 1953).

Q fever among Europeans in Nakuru is as a rule easily recognisable. The onset is sudden, and the characteristic features are rigors with drenching sweats, and intense headache. Cough is usual, and the sputum is often bloodstained, but these features are less constant than the rigors and headache. Malaria has always to be excluded, but Q fever can usually be distinguished by the fact that the rigors and profuse sweats often occur two or three times in twenty-four hours (see figure).




**Four-hourly temperature chart of case 8, showing six peaks of temperature in 60 hours. Pulse-rate did not rise above 96 during this period.**

Relative bradycardia is another valuable distinguishing feature.

In the past two years 9 cases with typical features and confirmatory complement-fixation titres have been encountered, and 4 more in which the diagnosis is probable, though the titre was below the level (1 in 100) which we have taken as conclusive (see table).

### Illustrative Case-report

A man, aged 33 (case 4 in table), felt perfectly well until the evening of Nov. 18, 1952, when he had a violent attack of shivering. He went to bed, felt hot, and sweated profusely. During the night he had another violent attack of shivering, followed by a rise of temperature and copious sweating. Next day he felt better though he still had fever. On the morning of the 20th he had another severe rigor with temperature 105°F, followed again by a drenching sweat. His temperature remained about 102°F until the morning of the 22nd when

DR. HALBRECHT: REFERENCES

Berblinger, W. (1946) *Schweiz. med. Wschr.* **76**, 1171.
Halbrecht, I. (1946) *Ibid.*, p. 708.
— (1951) *Lancet*, i, 85.
Liljedahl, S. O., Ryden, A. B. V. (1950) *Acta obstet. gynec. scand.* **30**, 359.
Schockaert, J. A. (1951) *Minerva ginec.* **3**, 507.
Sharman, A. (1944) *J. Obstet. Gynæc., Brit. Emp.* **51**, 85.
Sutherland, A. M. (1943) *Ibid.* **50**, 161.

ANALYSIS OF CASES

| Case no. | Age (yr.) | Sex | Occupation | Day after onset of illness on which serum was taken | End titre (1 in ... ) |
|---|---|---|---|---|---|
| 1 | 46 | F | Housewife | 186 | 200 |
| 2 | 40 | F | Housewife | 21 | 400 |
| 3 | 41 | M | Processing hides and skins | 15 | 800 |
| 4 | 33 | M | Clerk | 23 | 400 |
| 5 | 46 | F | Housewife | 31 | 400 |
| 6 | 45 | M | Farmer | 10 | 100 |
| 7 | 29 | M | Farmer | 10 | 80 |
| | | | | 62 | 200 |
| 8 | 32 | M | Agricultural officer | 12 | 400 |
| 9 | 36 | M | Clerk | 9 | 20 |
| | | | | 25 | 400 |
| 10 | 9 | M | Schoolboy | 23 | ±100 |
| 11 | 33 | M | Clerk | 14 | 50 |
| 12 | 47 | M | Dental surgeon | 14 | 40 |
| 13 | 23 | M | Farmer | 12 | 80 |

it was normal. The same evening, however, he had another rigor and his temperature rose to 103°F. It remained at this level for the next two days, rose to 104° on the 25th, and then fell by lysis over the following two days, after treatment with chlortetracycline (aureomycin) had been instituted. Throughout the illness he complained of very severe frontal headache with soreness of the eyes, backache, nausea, and anorexia. On the fourth day cough began, and next day his sputum was bloodstained. By this time prostration was considerable, and he was admitted to hospital.

On examination he looked very ill, was flushed, and had a moist skin and furred tongue. Temperature 102°F, pulse-rate 84. Crepitations were heard at the base of his left lung, but there were no other abnormal signs. The liver and spleen were not palpable. The white-cell count was 8000 per c.mm. (polymorphs 67%, lymphocytes 33%). No malaria parasites were seen. A chest radiograph showed no abnormality.

Q fever was diagnosed on the history and the relative bradycardia, and chlortetracycline therapy was started on the seventh day of the illness, 0·50 g. initially, followed by 0·25 g. eight-hourly to a total of 4 g. Recovery was rapid and convalescence normal, and the patient was discharged seven days after admission.

A sample of blood was taken on Dec. 11, twenty-three days after the onset, and sent by air-mail to Johannesburg, where a complement-fixation test with *R. burneti* antigen showed an end titre of 1 in 400, confirming the diagnosis of Q fever.

## Clinical Features

Most cases have conformed fairly closely to this picture, and in Nakuru an acute febrile illness with frequent shivering and sweating, intense headache, cough, and relative bradycardia is very probably Q fever and may be treated as such pending confirmation of the diagnosis, which can be made only retrospectively.

Besides the symptoms already mentioned, pain in the chest is sometimes complained of, and one patient complained bitterly of tenderness of the scalp. One patient had epistaxis, one had vomiting in addition to nausea, and nearly all complained of loss of appetite and constipation.

In a third of the cases the spleen was palpable. No patient had a palpable liver. Chest crepitations were audible in a third of the cases. In 3 cases these were localised to an area just above and lateral to the nipple, and in these patients radiography showed wedge-shaped peripheral shadows corresponding to the anterolateral segment of the upper lobe. No other cases showed abnormal radiological signs.

The total and differential white-cell counts were within normal limits in all the cases, but the total counts tended to be slightly lower than normal (case 4 was the one exception).

## Treatment

The response to chlortetracycline may be dramatic. The temperature falls within forty-eight hours, often within twenty-four hours, and subjective improvement is rapid. Chloramphenicol is also usually effective, but the response is slower, and in one case the illness responded only when chlortetracycline was substituted for the chloramphenicol (see figure). Chlortetracycline is the drug of choice; an initial dose of 0·50 g. followed by 0·25 g. eight-hourly to a total of 4 g. is usually adequate.

## Laboratory Studies

The diagnosis of Q fever may be established by the isolation of *R. burneti* from the patient's blood or urine during his acute illness. This may be effected by the inoculation of guineapigs or of embryonated eggs. These, however, are possible only in a specialised rickettsial-diseases laboratory. The final identification of a strain of rickettsia takes some considerable time and is fraught with the danger of infection of the laboratory staff. For these reasons it is usual and indeed preferable to rely on the results of serological tests to confirm a clinical diagnosis of Q fever. This was the method adopted in the present investigation. The sera sent from these patients were submitted to rickettsial complement-fixation tests with *R. prowazeki*, *R. mooseri*, *R. conori* var. *pijperi*, and *R. burneti* antigens.

It is desirable to compare the results of the tests on the acute-phase serum with those on the convalescent-phase serum. In Q fever, from being negative in the acute phase the test becomes positive in convalescence two to three weeks after the onset of the illness, usually in a titre of at least 1 : 100. Where no acute-phase serum is available the titre of complement-fixation given by the convalescent-phase serum is of considerable importance. Patients who have recently recovered from Q fever usually show a titre of at least 1 : 100. Conversely there is good reason to conclude that a patient whose serum gives a positive complement-fixation reaction with *R. burneti* antigen in a titre of more than 1 : 100 has recently had Q fever.

On the other hand, where Q fever is endemic, as it is in the Union of South Africa and (as this study has revealed) in East Africa, the sera of many people give a positive complement-fixation reaction in a titre of 1 : 10. No diagnostic significance can be attached to this finding except that such people have been infected with *R. burneti* in the past, possibly many years previously. It has been also observed that people with what we have called the hyperreactive auto-allergic diseases—e.g., acute lupus erythematosus—may give a complement-fixation reaction with *R. burneti* in a "diagnostic" titre of at least 1 : 100. A change in the result of the test from negative in the acute phase to positive in a titre of at least 1 : 100 in convalescence is therefore of greater significance than the result of a single test in convalescence. However, when such hyperreactive conditions can be ruled out, a positive complement-fixation reaction with *R. burneti* in a titre of 1 : 100 or higher is presumptive evidence that the patient's recent illness was Q fever. On this basis the serological tests (see table) show that in 9 of our cases the illness was Q fever, while in the other 4 it was probably Q fever.

## Discussion

These findings add Kenya to the list of countries in which Q fever is endemic. Before the second world war this disease was thought to be rare and confined to Australia and Montana, U.S.A. Since then it has been recognised in most countries, though its prevalence varies. It is commoner in the south and south-east of Europe than in the north-west.

In Africa Q fever has been identified in North Africa, in French Tropical Africa, and in the Ruanda Urundi province of the Belgian Congo. It was first diagnosed on serological findings in the Union of South Africa in 1949. Since then it has become apparent that it is the most prevalent rickettsial disease in southern Africa, where epidemic and murine typhus and tick-bite fever—the local variety of tick typhus—are also common (Gear 1954). Indeed it is so prevalent that most adult South Africans are immune, having been infected in childhood.

As the distinction between urban and rural life in South Africa increases, the incidence of Q fever in the older age-groups of the indigenous population may also

be expected to increase. Up to now, however, most of the cases in adults in South Africa have been observed in immigrants from north-west Europe. Many of these immigrants had, soon after their arrival, a febrile illness which was suspected on clinical grounds of being typhoid fever but proved on laboratory investigation to be Q fever. This infection was usually acquired, as in the present cases, from contact with an environment in which tick-infested cattle roamed. Some people contracted the infection soon after starting work on cattle or dairy farms, and others while visiting such farms. Usually the mode of infection seemed to be by inhaling dust contaminated with the causal rickettsiæ; more rarely it was from drinking infected milk. Q fever is thus one of the hazards that immigrants from north-west Europe face in southern Africa. The present study suggests that a similar hazard exists in East Africa or part of it.

Q fever may occur in explosive outbreaks like the one affecting students at the College of Art, Canterbury (Harvey et al. 1951), but is more commonly encountered as a sporadic infection, as in Nakuru.

Its occurrence here is no surprise, because it has been found in many parts of the world where the sources of human infection—cattle, sheep, and goats—exist and it has been looked for. These domestic animals excrete the rickettsiæ in their urine, fæces, and milk, and harbour them in their placentæ and fœtal membranes; hence human beings may be infected either by drinking milk or by inhaling dust, in which the rickettsiæ are remarkably persistent. Close contact—e.g., in delivering calves—may explain some cases.

In this East African community milk, dust, and contact with stock are all likely sources, and the next step will be to determine the source and route of the infection. Possibly more than one route is involved because whereas the consumption of cow's milk probably causes a large proportion of cases in the United Kingdom, contact with sheep, particularly the products of parturition, is a likely cause in the Romney Marsh area of Kent (Marmion et al. 1954).

Babudieri (1952) said, "It is now proved that if the virus has penetrated by inhalation there will be pulmonary localisation of the disease, and that there will not be pulmonary localisation if Coxiella has infected the organism through food, by subcutaneous injection, or through the surface mucous membranes." If this be true, dust-borne disease should be distinguishable from milk-borne disease.

Instances of case-to-case infection have been reported, notably in the small outbreak at the Royal Cancer Hospital, London (Harman 1949, Marmion and Stoker 1950), but are not common.

There appeared to be no connection between cases in this series, except in one instance:

Case 2 became ill on Nov. 3, 1952, and her husband (case 3) on Nov. 18, fifteen days later. Both could have been infected from a common source, but possibly the wife infected her husband. The husband was employed in processing hides and skins; and, had his wife not been taken ill first, it would have been tempting to attribute his illness to his occupation.

It has not been possible so far to control the infection among stock; but while Q fever remains sporadic and amenable to chemotherapy the problem does not seem urgent. However, the pasteurisation of milk, which at present is on the borderline of effectiveness in killing the rickettsiæ, might perhaps be modified to provide a a wider margin of safety.

### Summary

During the past three years several patients with an acute febrile illness, characterised by frequent rigors and sweats and intense headache, have been seen in Nakuru, Kenya. Many have had cough and hæmoptysis, and some of these have provided radiological evidence of segmental pneumonia.

The clinical diagnosis of Q fever was confirmed in 9 of these cases by finding that the rickettsial complement-fixation test gave a positive result with *R. burneti* antigen in a titre of 1 : 100 or higher, whereas the test with other rickettsial antigens gave negative results.

In 4 other cases the results suggested Q fever but the titre of complement fixation did not reach 1 : 100.

These findings add Kenya to the list of countries in which Q fever is endemic, and this disease is one of the minor hazards for immigrants from north-west Europe to South and East Africa. Its occurrence in East Africa was to be expected because the usual sources of human infection—cattle, sheep, and goats—are found there in large numbers.

### REFERENCES

Babudieri, B. (1952) World Health Organisation: Monograph Series no. 19, p. 165.
Gear, J. (1954) *S. Afr. J. clin. Sci.* 5, 158.
Harman, J. B. (1949) *Lancet*, ii, 1028.
Harvey, M. S., Forbes, G. B., Marmion, B. P. (1951) *Ibid*, ii, 1152.
Marmion, B. P., Stewart, J., Richmond, P., Barber, H., Stoker, M. G. P. (1954) *Ibid*, i, 1288.
— Stoker, M. G. P. (1950) *Ibid*, ii, 611.
— — McCoy, J. H., Malloch, R. A., Moore, B. (1953) *Ibid*, i, 503.

## BLOOD-COAGULATION DEFECT ASSOCIATED WITH MISSED ABORTION

D. T. O'DRISCOLL
M.D., M.A.O. N.U.I.
CONSULTANT GYNÆCOLOGIST, WESTERN HEALTH COMMITTEE, GALWAY

S. M. LAVELLE
M.B. N.U.I.
IRISH MEDICAL RESEARCH COUNCIL FELLOW, DEPARTMENT OF PATHOLOGY, UNIVERSITY COLLEGE, GALWAY

CERTAIN complications of pregnancy have assumed new importance with the recent recognition of the fact that they may be accompanied by disorders of blood coagulation which if not properly treated may prove fatal.

Blood-coagulation defects have now been found in accidental hæmorrhage, amniotic embolism, retention of a dead fœtus, induced abortion, and toxæmias of pregnancy and as a cause of delayed postpartum hæmorrhage (Maisel et al. 1954). In fact the present position is such that any case in which bleeding per vaginam continues for no apparent reason after delivery must be regarded as probably due to a blood-clotting defect, and attempts to ascertain the particular defect by suitable blood tests are more likely to be rewarding than continual local attempts at hæmostasis. This subject has been fully reviewed by Ratnoff et al. (1955).

Accidental hæmorrhage and retention of a dead fœtus are comparatively frequent complications of pregnancy, and it is of the utmost importance that anybody undertaking the care of the expectant mother be aware of the possibility that a hæmorrhagic state may develop as a further complication in these cases. This is especially important in the case of missed abortion, where domestic treatment is often undertaken.

The so-called acquired fibrinopenia of accidental hæmorrhage has been very fully described, but the occurrence of severe defects of blood coagulation in missed abortion has not long been recognised, and only a handful of cases have been described in any detail.

### Ætiology

This disorder of the blood is most likely to develop where the death of the fœtus has been due to iso-immunisation of the mother by Rh antigen and where the fœtus has attained the age of sixteen weeks; but it can develop without iso-immunisation of the mother and as early in pregnancy as the eighth week (Barry et al. 1955). It seems, however, that the dead fœtus must be necessarily retained for at least four weeks for the disorder to develop, unless the position is further complicated

RESULTS OF COAGULATION TESTS

| Specimen taken on | Pro-thrombin-time (sec.) | Platelets per c.mm. | Lysis time of clot (min.) | Thrombo-plastin-heparin time | Anti-thrombin (%) | Thrombin-time (% of normal) | Pro-thrombin (%) | Fibrinogen (mg. per 100 ml.) |
|---|---|---|---|---|---|---|---|---|
| June 11 .. .. .. | — | — | Nil | — | 60 | — | — | 250 |
| July 18 at 5.15 P.M. .. | 19·5 | 77,000 | 70 | 5–30 min. | 55 | 115 | >100 | 31 |
| July 18 at 7.45 P.M. .. .. | No clot | — | <240 | — | 85 | 130* | >100 | Nil |
| July 18 at 9 P.M. .. .. | 15 | — | Partial 180 | — | 72 | 112·5 | >100 | 145 |
| July 18 at 10.30 P.M. .. | 15 | 126,000 | 120 | 4–6 min. | 72 | 125 | >100 | 145 |
| July 19 at 4.15 P.M. .. .. | 13 | 60,000 | Nil | 105 sec. | 100 | 73 | — | 250 |
| July 20 at 11 A.M. .. .. | 14 | 108,000 | Nil | 71 sec. | — | — | — | Normal |
| July 29 at 3 P.M. .. .. | 13 | 260,000 | Nil | 73 sec. | 90 | Normal | — | 405 |

* With fibrinogen added to sample and control.

by abruptio placenta, when it may occur very suddenly (Schneider 1953).

In this later type of case the ætiology is similar to abruptio placenta where the fœtus is alive.

Retention of the dead fœtus for some time seems to indicate that the agent causing the disorder comes from the contents of the pregnant uterus, and that a certain length of time is necessary to allow of its production and/or its influence on the maternal circulation.

Lysis of the blood-clot in an abnormally short time when kept at 37°C is a common accompaniment. This is rare in the fibrinopenia of accidental hæmorrhage. Evidence for the presence of a fibrinolytic agent is contradictory:

Vecchietti (1953) observed that the amniotic fluid of a patient whose fœtus had been dead for some weeks was fibrinolytic.

Ratnoff et al. (1955) could not detect any significantly abnormal fibrinolytic activity in the blood of five patients with hypofibrinogenæmia associated with missed abortion, and Pritchard and Ratnoff (1950) did not detect fibrinolytic activity in the amniotic fluid in two cases.

Reid et al. (1953) suggest that the fibrinogen is consumed by intravascular coagulation possibly due to the thromboplastin produced by the degenerating placenta. This suggestion has been adopted to explain secondary postpartum hæmorrhage associated with blood-coagulation defect (Maisel et al. 1954).

## Case-report

A woman, aged 37, had had eleven previous pregnancies, all of which had ended in live births. The third infant died with jaundice three days after birth. The eighth infant was deeply jaundiced at birth and died at seven weeks. The ninth infant was deeply jaundiced within nine hours of birth; an exchange transfusion was given, but the infant died at $7^1/_2$ months. The eleventh infant was born on Aug. 1, 1954, at term; it was œdematous and became jaundiced very rapidly and did not survive many hours after exchange transfusion. Its Hb was 9·1 g. per 100 ml., its blood-bilirubin level was 9·5 mg. per 100 ml., and a blood-film contained 80% of nucleated red cells. Towards the end of this pregnancy the patient had become grossly œdematous, especially in her legs, over her sacrum, and in her abdominal wall, and became rapidly more so in the week preceding labour.* There was no albuminuria, and the blood-pressure remained within normal limits. The patient was not seen again until April 21, 1955, when she had had no menses since her last pregnancy and thought that she was about twenty weeks pregnant. She had just felt movement two weeks previously and still felt movement. On examination the size of the uterus indicated a pregnancy of about twenty-two to twenty-four weeks, and the fœtal heart was heard. The antibody titre at this stage was 1 : 128.

*May 21, 1955.*—The patient reported that she had not felt movement for about two weeks. The fœtal heart-beat was absent. The patient being very anxious to have labour induced, she was given ethinylœstradiol 1 mg. every waking hour for a week and then given an oxytocin drip induction (5 units of oxytocin to each pint of glucose solution, 120 drops a minute). This was run for eight hours on three successive days; and, although violent uterine contractions occurred, the cervix remained firmly closed and uneffaced. The patient was then discharged at her own request and was asked to return at weekly intervals or immediately if she noticed spontaneous bleeding from any site.

*June 16, 1955.*—The blood-fibrinogen level was 250 mg. per 100 ml., clot retraction normal, clot stable for twenty-four hours at 37°C, and serum-antithrombin level 60%. No abnormality was noted. (For the techniques used in this investigation see Appendix.)

*July 18, 1955.*—The patient was seen at 4.30 P.M. She had not been seen since June 16 despite warning. She now complained that she had felt a sharp sting in her thigh during the previous night and noticed that she had developed a large spontaneous bruise, and others had appeared within the last few hours. Three large bruises were visible on her arm and thigh and several small bruises on her legs. At 5.15 P.M. her bleeding-time was 1 min. 10 sec. and clotting-time 8 min. 10 sec., and a tourniquet test produced a fine crop of petechiæ in 6 min. at 100 mm. Hg (positive result). The one-stage prothrombin-time estimated within 10 min. of venepuncture was 19·5 sec., only a minimal clot being present, and this time was reduced to 15 sec. by the addition of 20% of normal plasma, and to 13 sec. by the inclusion of fibrinogen. The time was not significantly reduced by the addition of serum or of absorbed plasma. The fibrinogen reading of 31 mg. per 100 ml. is probably low, the sample having become lysed during the 30-min. delay between venepuncture and clotting the aliquot with thrombin. Heating the plasma to 56°C for 6 min. and 25% saturation with ammonium sulphate produced very small precipitates in comparison with the control. The platelet-count by the direct method was 77,000 per c.mm. and the hæmatocrit 40%. Clot retraction was brisk, but the clot showed lysis at 30 min. and was gone in 70 min. in two of the clotting-time tubes. In the other tube the clot did not altogether disappear. Recalcified thrombin-precipitated clots, buffer-diluted 1 in 8, 16, and 32, lysed between 60 min. and 150 min. after clotting at 37°C. The thromboplastin-heparin time was 5–30 min. and was not shortened by the addition of fibrinogen. The control time was 95 sec. The addition of 20% of patient's heparin plasma to the control prolonged the control time to 123 sec., indicating anticoagulant activity at this level. The prothrombin-consumption index 75 min. after clotting was 30%, antithrombin 55%, and two-stage prothrombin-time well over 100%, normally accelerated.

*Hysterectomy.*—A decision was made to attempt at least partial correction of the coagulation defect by transfusing four pints of dried plasma in one pint of distilled water (pure fibrinogen was not available) and to do a closed hysterectomy if this produced the anticipated improvement. Since only eight pints of plasma was available, it was decided that immediate removal of the source of the offending agent was of the gravest urgency. At 7.45 P.M. a specimen of blood was taken before the infusion of concentrated plasma and was tested six hours later in common with two succeeding specimens. The citrated sample was kept at room-temperature and the clotted blood at body-temperature. In the interval the clot had lysed completely. There was no fibrinogen in the citrate sample, no precipitate following the addition of thrombin or heating to 56°C for 6 sec. or precipitation after 33% saturation with ammonium sulphate. The prothrombin-time with fibrinogen added was 13 sec. Two-stage prothrombin estimation was much greater than 100%, antithrombin 85%, and thrombin-time with fibrinogen 37 sec. compared with a control time of about 28 sec. The serum added to normal clotted blood did not effect lysis after twelve

* We have now observed rapidly developing œdema on other occasions in severe cases of iso-immunisation of the mother without evidence of pre-eclampsia; and this is characteristic of the presence in the uterus of a severely affected fœtus. The œdema may have an allergic basis; it clears rapidly after the birth of the infant.

hours' incubation at 37°C. At 9 P.M. the first pint of quadruple-strength concentrated plasma had been infused and the operation was due to start. Some lysis of the clot took place, but a small nidus remained stable for twenty-four hours. The 1 in 32 dilution clot did not lyse. Prothrombin-time was 15 sec. (14 sec. with fibrinogen added). The two-stage prothrombin-time was well over 100% but not so high as before. The fibrinogen level was 145 mg. per 100 ml., a precipitate being present from heating to 50°C for 6 min. and on 33% saturation with ammonium sulphate. Antithrombin was 72%. Thrombin-time was 27 sec. compared with 24 sec. in the control, and the addition of fibrinogen prolonged it to 30 sec. compared with 28 sec. in the control.

*Postoperative Course.*—At 10.30 P.M. the operation was over, and a pint of blood had been infused. No undue bleeding was experienced during the operation, but there were fresh petechial hæmorrhages on the surface of the uterus; so a further pint of quadruple-strength plasma was transfused. The blood clotted, and the clot lysed completely in two hours at 37°C. The 1 in 32 dilution clot did not lyse in twelve hours at 37°C. The prothrombin-time was 15 sec. with a poor clot, and 13 sec. when fibrinogen was added. Two-stage prothrombin estimation was slightly higher than in the previous specimen. The fibrinogen level was 145 mg. per 100 ml., and a precipitate was present on heating to 56°C for 6 min, and on 33% saturation with ammonium sulphate. Antithrombin was 72%, and the thrombin-time 32 sec. compared with 24 sec. in the control, and 38 sec. compared with about 28 sec. in the control when fibrinogen was added. The thromboplastin-heparin time was 240–300 sec. When fibrinogen was added it was 240 sec. The platelet-count was 126,000 per c.mm. At 11 A.M. next day the prothrombin-time was normal, no lysis was present, the fibrinogen level was 250 mg. per 100 ml., antithrombin was 100%, there were 60,000 platelets per c.mm., the thromboplastin-heparin time was 105 sec. compared with 95 sec. in a control, and the thrombin-time was 28 sec. compared with 38 sec. in a control. On the second postoperative day the prothrombin-time was 14 sec., the fibrinogen level was within the normal range, no lysis was observed, the thromboplastin-heparin time was 71 sec., and there were 108,000 platelets per c.mm. On the eleventh day the prothrombin-time was 13 sec., the fibrinogen level was 405 mg. per 100 ml., the antithrombin was 90%, the thrombin-time was 31 sec, compared with 32 sec. in a control, the thromboplastin-heparin time was 63 sec. compared with 67 sec. in a control, and there were 260,000 platelets per c.mm. (see table).

*Pathological Report* (Prof. J. Kennedy).—The uterus showed multiple hæmorrhages beneath the serosa and contained a macerated fœtus measuring about 7 in. from crown to rump. There was no gross retroplacental hæmatoma. No histological detail could be made out in the fœtus owing to maceration. The placenta histologically showed old and recent infarcts. There were many areas of calcification within the villi. Two areas of giant-cell reaction were present. No immature blood-forming cells were seen. The placental villi retained their thromboplastic covering. It was impossible to diagnose erythroblastosis from the placenta.

## Discussion

The features of the case are active fibrinolysin, thrombocytopenia, plasma hyposensitivity to bovine thrombin, and hypofibrinogenæmia. The lysis, the hypofibrinogenæmia, and the thrombin hyposensitivity improved after the infusion of concentrated plasma and disimproved after the substitution of blood for the plasma during the operation. The platelets were not counted immediately before the operation, but after it the count was raised above normal. Next morning all was normal save the platelet-count and a slightly prolonged thromboplastin-heparin time, and thrombin hypersensitivity had superseded the hyposensitivity. Further progress was uneventful. The rapidity of the lysis of the first specimen was such that immediate infusion of concentrated plasma and surgical removal of the presumable cause seemed advisable. The lysin was inactivated either by time or by the citration-recalcification process, or by normal blood. Probably the fibrinogen level in the 5.15 P.M. and 7.48 P.M. specimens was higher at the moment of venepuncture and the fibrinogen underwent lysis before being estimated. A definite anticoagulant effect at the thromboplastin-heparin level seems to have been exercised by the 5.15 P.M. sample. The fibrinogen level in this type of case may fall gradually over some weeks (Ratnoff et al. 1955). If that happened in the present case, the development of the thrombocytopenia must be of grave import and of the lytic activity decisive.

The treatment of missed abortion takes on a new importance with the recognition of the fact that a blood-coagulation defect may develop. The rapidity with which the hæmorrhagic state develops, once the disorder is initiated, means that one must be prepared to deal with this grave emergency. For many years the standard treatment of missed abortion has been one of expectancy, because of the unreliability of the methods of induction of labour and the grave danger of infection.

The mental anguish of a patient condemned to carry a dead fœtus in her abdomen must be very great. Now that we have the additional stimulus that a defect of coagulation can develop, the balance is decidedly in favour of emptying the uterus as soon as the intra-uterine death has been verified. Before the twelfth week evacuation by dilatation and curettage will not present any great difficulties; after the twelfth week the correct method will require careful consideration.

Oxytocin-drip induction is the method of choice, but that this is not always successful is illustrated by the present case. The method most likely to succeed is the introduction of a stomach-tube into the uterus. This should be done with scrupulous attention to asepsis, and the patient should be kept under an antibiotic umbrella while awaiting the onset of labour. Rarely will the tube have to be removed at the end of seventy-two hours because labour has not taken place. If this method fails, the patient must be kept under strict surveillance, samples of her blood should be examined frequently, and hysterotomy should be done after a transfusion of either concentrated plasma or pure fibrinogen at the earliest sign of defective coagulation of the blood. The beneficial effect of concentrated plasma on the various types of coagulation defect seen in obstetrical and surgical bleeding is discussed elsewhere (Lavelle 1955).

## Summary

A case of blood-coagulation defect complicating missed abortion is presented in which active fibrinolysis, thrombocytopenia, plasma hyposensitivity to bovine thrombin, and hypofibrinogenæmia were the main features.

Attention is drawn to the danger of treating these cases in domestic practice, unless one is equipped to deal with a grave defect in blood coagulation.

The standard treatment of missed abortion should be induction of labour at the earliest possible moment after confirmation of intra-uterine death of the fœtus.

The efficiency of concentrated plasma in the treatment of these cases is illustrated.

### APPENDIX

Blood was taken by venepuncture with an oiled syringe and citrated 9 parts to 1 part of 3·8% sodium-citrate solution.

Plasma was separated by centrifugation at 3000 r.p.m. for 5 min.

Clotting-time was estimated by the Lee-White method, the mean of three tubes being taken, and bleeding-time by the Duke method, the mean of both ears being taken.

The Quick one-stage prothrombin-time with rabbit-brain thromboplastin gave a normal time of 13 sec., and fibrinogen was added as 0·1 ml. of a saline solution containing bovine fibrinogen 200 mg. per 100 ml. before recalcification. 1 ml. of blood was incubated at 37°C for examination of clot retraction and lysis.

Thrombin-time was estimated with 0·1 ml. of thrombin dilution added to 0·2 ml. of citrated plasma at 37°C to give a normal time of about 30 sec.

Fibrinogen was estimated by King's (1951) method. Platelets were counted by a direct method from blood in

Wintrobe silicone tubes. Dilution clots for lysis, two-stage prothrombin-time, and prothrombin-consumption index were according to the methods of Biggs and Macfarlane (1953). Serum antithrombin was estimated according to MacFarlane (1952).

Thromboplastin-heparin time: 3 ml. of blood was added to 9 units of heparin previously dried in a test-tube, and well mixed. After separation 0·2 ml. of plasma was timed to clot with 0·1 ml. of standard thromboplastin solution. The time for normals is constant for a given batch of heparin and thromboplastin. It is believed that the test measures heparin sensitivity at the prothrombin level.

Adsorbed plasma was prepared by adding 0·1 ml. of aluminium hydroxide gel to 1 ml. of plasma, incubating at 37°C for 5 min., and separating plasma by centrifugation. This plasma gave a quick prothrombin-time of 50–70 sec.

The work of one of us (S. M. L) was financed by the Medical Research Council of Ireland, and was carried out in the department of pathology, University College, Galway.

REFERENCES

Barry, A. P., Geoghegan, F., Shea, S. M. (1955) *Brit. med. J.* ii, 287.
Biggs, R., Macfarlane, R. G. (1953) Human Blood Coagulation and its Disorders. Oxford.
King, E. J. (1951) Microanalysis in Medical Biochemistry. London; p. 44.
Lavelle, S. M. (1955) *Irish J. Med. Sci.* (in the press).
MacFarlane, J. C. W. (1952) *Lancet*, ii, 311.
Maisel, F. J., Cartnick, E. N., Zaino, E. C. (1954) *Obstet. Gynec.* 3, 204.
Pritchard, J. A., Ratnoff, O. D. (1950) *Surg. Gynec. Obstet.* 60, 1015.
Ratnoff, O. D., Pritchard, J. A., Colopy, J. E. (1955) *New Engl. J. Med.* 253, 63.
Reid, D. E., Weiner, A. E., Roby, C. C., Diamond, L. K. (1953) *Amer. J. Obstet. Gynec.* 66, 500.
Schneider, C. L. (1953) *Obstet. Gynec.* 1, 321.
Vecchietti, G. (1953) *Riv. Obstet. Ginec.* 8, 443.

# CONGENITAL TOXOPLASMOSIS

## DIAGNOSIS CONFIRMED BY PASSAGE TO MOUSE

D. MORRIS
M.R.C.P., D.C.H.
CLINICAL RESEARCH-WORKER

B. LEVIN
B.Sc., M.D., Ph.D. Lond.
CONSULTANT PATHOLOGIST

N. E. FRANCE
M.B. Wales
CONSULTANT PATHOLOGIST

QUEEN ELIZABETH HOSPITAL FOR CHILDREN, LONDON

THE cardinal clinical features of congenital toxoplasmosis—meningo-encephalo-myelitis, chorioretinitis, and radiological evidence of cerebral calcification—are sufficiently well recognised to enable a good proportion of cases to be diagnosed at or soon after birth. Purpura in a newborn infant, although more commonly associated with other conditions, is occasionally one of the presenting features of toxoplasmosis. Callahan et al. (1946) noted purpura in 3 of 18 cases.

In the case reported here purpura was the earliest abnormality seen, but until the ocular signs were observed, the possibility of toxoplasmosis was not appreciated.

The diagnosis of toxoplasmosis has hitherto usually been confirmed either by serological tests or by detecting *Toxoplasma gondii* microscopically post mortem. Valentine et al. (1953) reported for the first time in this country the successful passage of the parasite to a mouse from a case of congenital toxoplasmosis; this has since been accomplished by H. S. Baar, and by C. P. Beattie (personal communications) in 3 further cases. Owing to the rarity with which the organism has been isolated in this country from human material this further case is reported.

### Case-report

A female infant was born at term to a primiparous woman aged 23, at the Military Families Hospital, Woolwich. The mother had no history of past illness, and her pregnancy was uneventful. The child was born by spontaneous delivery and weighed 6 lb. 9 oz. At birth the baby was moderately shocked but required no special resuscitation. Purpuric spots were present over her face and trunk, and vitamin K was given during the next 24 hours. She became fretful, refused feeds, and looked unwell; fresh purpura appeared over her body. At the age of 36 hours she was transferred to the British Hospital for Mothers and Babies, and thirteen days later to the Queen Elizabeth Hospital for Children.

*On admission* she was pale and mildly dehydrated, her muscle tone was poor, and her cry feeble and high-pitched. The purpura affected mostly her face and trunk; her liver and spleen were easily palpable, both extending about 3 inches below the costal margins.

*Treatment and Progress*

The infant was nursed in an oxygen tent, fed with expressed breast-milk by œsophageal tube, and given penicillin 100,000 units and streptomycin 100 mg. twice daily for four days. Chloral hydrate gr. 1 was given as required. The purpura gradually faded, and the spleen was no longer easily felt by the 5th day of life, although the liver remained palpable. In spite of a daily intake of 50 calories per lb. of body-weight her weight decreased from 6 lb. 9 oz. to 5 lb. 13 oz. Later, when fluids were taken with difficulty by mouth they were augmented by subcutaneous and intravenous infusions. Irritability, which had been mild at the onset, gradually increased, and generalised convulsions ensued. The cranial sutures were observed to have separated, although the circumference of the head remained unaltered at 13½ inches. Both eyes were microphthalmic; ophthalmoscopy revealed a large white opacity in the left lens and a smaller one in the right lens. The baby's condition slowly deteriorated, convulsions came on with increasing frequency and proved more difficult to control, and she died at the age of 25 days.

Fig. 1—Coronal section through left cerebral hemisphere, showing extensive necrosis around lateral ventricle.

*Investigations*

Examination of her blood showed Hb 15·6 g. per 100 ml., red cells 5,200,000 per c.mm., colour-index 0·96, leucocytes 13,000 per c.mm. (polymorphs 66%, eosinophils 3%, lymphocytes 29%, monocytes 2%), platelets 260,000 per c.mm., prothrombin-time normal, blood-urea level 97 mg. per 100 ml., plasma-bilirubin level 0·7 mg. per 100 ml., blood-group $A_1$ Rh-positive to anti-D, and Wassermann, Kahn, and gonococcal complement-fixation tests negative. The cerebro-spinal fluid (C.S.F.) was xanthochromic and contained 28 cells per c.mm. (polymorphs 4%, lymphocytes 96%), total protein 825 mg. per 100 ml., and chlorides 770 mg. per 100 ml. The Pandy globulin test was positive. No toxoplasma cells were seen on microscopy of the fluid. Radiographs of the skull showed small areas of cerebral calcification and widening of the sutures. Toxoplasmic encephalitis having been provisionally diagnosed, Dr. I. A. B. Cathie examined the blood and obtained the following results:

| | *Dye-test titre* | *Complement-fixation test titre* |
|---|---|---|
| Mother .. .. .. | 1 in 64 | 1 in 128 |
| Infant .. .. .. | 1 in 8 | Negative |

and reported that "the positive dye test in the baby is presumably passive transference."

*Necropsy Findings*

A well-nourished female weighing 6 lb. 13½ oz. and measuring 20 inches in length. The circumference of the head was 14 inches; there was no separation of the sutures. Both eyes were microphthalmic, and there was an apparent opacity of the left lens. The brain (427 g.) had a normal gyral pattern, with flattening of all gyri and widening of the sulci. About twelve irregular slightly depressed firm pale-yellow areas with thickening of the overlying lepto-

Fig. 2—Cortical lesion showing peripheral calcification and central necrosis with cellular exudate in leptomeninges. (Hæmatoxylin and eosin. ×34.)

meninges were seen on the surface of both cerebral hemispheres. Some were only a few millimetres in diameter; the largest, around the right calcarine fissure and on the left occipital lobe, measured 18 × 12 mm. and 18 × 9 mm. Section of these areas showed firm pale-yellow punctate tissue extending 3–6 mm. into the substance of the cortex and sharply demarcated from the surrounding tissue. A sagittal section through the brain showed the entire corpus callosum, fornix, lamina terminalis, hypothalamus, pineal body, and septum lucidum to be friable, yellowish-brown, and obviously necrotic. The third ventricle was filled by a recent blood-clot. The pituitary gland appeared normal. Coronal sections through the left cerebral hemisphere (fig. 1) showed moderate dilatation of the lateral ventricle, which was lined to a depth of 3–6 mm. by a zone of reddish-brown granular gritty tissue. The anterior thalamus was speckled with numerous calcified spots; this appearance extended for 1–2 cm. lateral to the lining of the third ventricle and involved the basal ganglia but not the putamen and insula. Anteriorly in the white matter of the left temporal lobe was an area of softening with a cavity measuring 3·4 × 3·0 × 1·4 cm.³ and lined by soft grey tissue; it did not communicate with the inferior horn of the lateral ventricle. Here and there small soft brown areas resembling early necrosis were visible in the white matter of the hemisphere. No abnormalities were seen in the cerebellum, brain stem, or spinal cord, and all other organs appeared normal.

*Histology*

The lesions in the cerebral cortex showed central necrosis with powdery calcification often appearing to have arisen by deposition of calcium salts in necrotic nerve-cells (fig. 2). At the periphery was a zone of large irregular polygonal or oval cells with vesicular nuclei and pale-staining cytoplasm together with a few lymphocytes, occasional compound granular corpuscles, and a little glial proliferation. Numerous toxoplasma cells, intracellular, extracellular, and in the form of pseudocysts, were found in this tissue (figs. 3 and 4). The overlying meninges were infiltrated by mononuclear cells and lymphocytes. Early cortical lesions consisted of epithelioid cells, lymphocytes, and neuroglia but showed no calcification. The lining of the ventricular system showed a cellular reaction with numerous toxoplasma cells adjacent to normal brain tissue and separated from the ventricle by a zone of necrosis and calcification. The cavity in the left temporal lobe was lined by necrotic brain tissue with no accompanying inflammation. Small lesions were present in the dentate nucleus and throughout the brain stem and spinal cord. A particularly large calcified focus was situated in the lumbar cord. The membranes covering the brain stem and spinal cord were infiltrated by a few mononuclear cells and lymphocytes. Dr. N. Ashton reported that the right eye showed posterior synechiæ and a delicate inflammatory pupillary membrane with a normal lens and ciliary body. There was focal chorioretinitis with destruction of the retina, considerable pigmentary disturbance, and inflammatory infiltration of the choroid and vitreous. Near the disc granulation tissue extended into the vitreous, and there was a folded retinal detachment. Numerous extracellular and intracellular toxoplasma cells were seen in the retina. The optic nerve was normal. The left eye showed similar but more severe chorioretinitis with mild inflammatory infiltration of the ciliary body and early cataractous changes in the posterior cortex of the lens. Since the ocular contents were completely formed and there were no persisting fœtal structures, Dr. Ashton considered the microphthalmia to be the result of the endophthalmitis rather than of an arrest of growth, and he suggested that the inflammation was not fully established until the last weeks of pregnancy. Apart from accidental involution of the thymus, all other organs were normal.

**Passage of Toxoplasma from Brain to Mouse**

A portion of the brain from the edge of a large necrotic area removed at necropsy was made into a fairly fine suspension by grinding in a test-tube in about ten times its volume of broth with a glass rod. The suspension was inoculated into three mice, one intracerebrally with 0·01–0·02 ml. and two intraperitoneally with 0·3–0·4 ml. From the first mouse no toxoplasma was obtained despite several attempted passages into further mice.

One of the two mice injected intraperitoneally became ill and was killed twelve days after injection. About

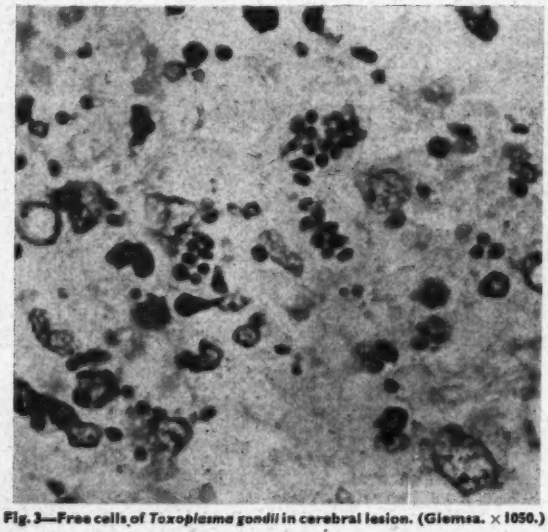


Fig. 3—Free cells of *Toxoplasma gondii* in cerebral lesion. (Giemsa. × 1050.)

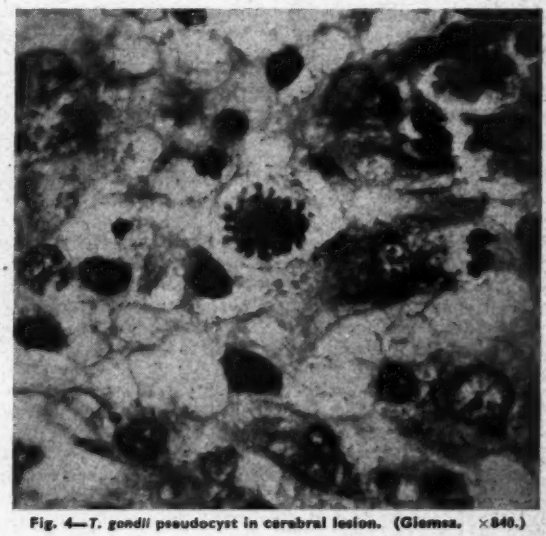


Fig. 4—*T. gondii* pseudocyst in cerebral lesion. (Giemsa. ×840.)

0·5 ml. of a turbid fluid was found in the peritoneal cavity, but careful search, after staining, failed to reveal the parasite. The remainder of the fluid was inoculated into two other mice, one intracerebrally and the other both intracerebrally and intraperitoneally. The first was sacrificed after seventeen days and showed no evidence of encephalitis; nor did mice inoculated with its brain suspension. The other mouse became ill and died twelve days after injection. Its mucoid peritoneal fluid showed numerous free toxoplasma cells; from this there was no difficulty in continuing passage by the intraperitoneal route.

Mice inoculated with peritoneal washings from the last of the original three mice were accidentally killed two days after injection; hence this passage was lost.

Some of the original suspension was also inoculated into developing hen's eggs by Prof. C. F. Barwell. After eight days lesions were obtained on the chorio-allantoic membrane, and scanty free toxoplasma cells were found.

### Discussion

That many species of mammals and some birds are infected with toxoplasma has been well established (Feldman 1954), but whether this animal reservoir of infection is the source of human toxoplasmosis is uncertain. It seems worth while to assess the significance of animal contact in every case of active human infection. Dr. R. Lainson, who investigated the epidemiology of the present case, found that the mother had been in Egypt for thirteen months and became pregnant five months after her return to this country. She worked in a hospital canteen for the first sixteen weeks of pregnancy and, after a break of two months spent in Cardiganshire and South London, she returned to her original occupation in Woolwich until shortly before the birth of the infant. A considerable number of cats, some of them having the run of the kitchens, stores, &c., had access to the canteen; one of these was her particular pet, and she also kept a cat in her home both in Woolwich and Wales. The mother admitted that she was in the habit of petting and caressing any dog or cat which presented itself, and she did not mind their licking her hands and face. She said that she was "subject to insect bites." She did not in her work prepare food; she never handled rabbits, alive or dead. Since the number of contacts with animals was so great, it was impossible to single out any one animal for examination as the source of infection.

Sabin (1953) has followed over 50 mothers none of whom produced an infected child subsequently. He suggests that the fœtus is infected only when the mother is in an acute infective state, which may be inapparent or unrecognised. In the present case, five months after the birth of the patient the mother aborted in the seventh week of pregnancy. The fœtus was examined microscopically and showed no evidence of toxoplasmosis; the placenta was normal.

Some petechiæ are commonly found over the presenting part after normal deliveries, particularly if there has been delay in the delivery and local cyanosis is present. Generalised purpura in a newborn infant is a diagnostic problem. Generalised infection, thrombocytopenia, hæmorrhagic disease, and blood-group incompatibility may be excluded by examination of the blood. With no abnormal findings in the blood the possibilities narrow to less common conditions, such as cytomegalic inclusion disease and toxoplasmosis. Examination of the C.S.F. may help. There are few conditions in which the protein content of the C.S.F. is much raised with only a relatively small increase in the cell-count. This is always the case with a spinal tumour and block and sometimes with a cerebral tumour, lead encephalopathy, and a subdural hæmatoma. To these should be added toxoplasmic encephalitis. A xanthochromic C.S.F. with a considerable excess of protein and only a slight or moderate increase in cells, as in the present case, suggests toxoplasmosis.

Although there was active infection, the infant gave a negative complement-fixation test. Such a finding is not infrequent (Feldman 1954) and should not exclude a diagnosis of toxoplasmosis.

None of us had had any previous practical experience of toxoplasma; so the relative ease with which it was isolated will perhaps encourage others to investigate all cases of suspected toxoplasmosis. In the present instance, only intraperitoneal passage into mice was successful; none of the mice inoculated intracerebrally developed encephalitis or showed parasites on histological examination. Intraperitoneal inoculation is simple and appears sufficient. No toxoplasma cells were seen in the intraperitoneal fluid in the first transfer to mice, but such a finding should not deter an attempt at a second or even third passage before assuming a negative result.

Finally, although it was impossible to trace the source of infection in the present case, since toxoplasmosis is common among domestic animals (Feldman 1954) pregnant women should be warned to avoid close contact with them.

### Summary

A fatal case of toxoplasmic encephalomyelitis and chorioretinitis in a newborn infant is described, and its epidemiology is discussed.

Toxoplasma cells obtained from the infant's brain after death were passed by intraperitoneal inoculation to mice.

Purpura may be a presenting sign of toxoplasmosis.

A considerable excess of protein and a relatively small excess of cells in the C.S.F. is of diagnostic significance.

We are indebted to Dr. R. H. Dobbs for his permission to publish the clinical details; Major B. W. Hughes for referring the case to us; and Mrs. F. M. Byron and Mr. G. Hunt for their technical assistance.

### REFERENCES

Callahan, W. P. jun., Russell, W. O., Smith, M. G. (1946) *Medicine, Baltimore*, **25**, 343.
Feldman, H. A. (1954) *In* Nelson, W. E. Textbook of Pediatrics. 6th ed., Philadelphia and London; p. 605.
Sabin, A. B. (1953) *Amer. J. trop. Med.* **2**, 360.
Valentine, J. C., Lane, W. F., Beattie, C. P., Beverley, J. K. A. (1953) *J. clin. Path.* **6**, 253.

## THE FAILURE OF ACETYLATION IN DIABETIC COMA

F. NAVAZIO, ASSISTANT
N. SILIPRANDI, ASSISTANT PROFESSOR
INSTITUTE OF BIOLOGICAL CHEMISTRY, UNIVERSITY OF ROME, ITALY

HUMAN, rabbit, and rat blood can acetylate *p*-aminobenzoic acid and sulphanilamide in vitro (Blondheim 1955). This finding makes it easier to investigate acetyla-

ACETYLATION BY BLOOD OF HEALTHY PEOPLE AND OF DIABETICS

| Healthy people | | Diabetics | | Patients in diabetic coma | |
|---|---|---|---|---|---|
| Person no. | Percentage of acetylated sulphanilamide | Case no. | Percentage of acetylated sulphanilamide | Case no. | Percentage of acetylated sulphanilamide |
| 1 | 17·6 | 1 | 14·3 | 13 | 0·10 |
| 2 | 15·9 | 2 | 25·2 | 14 | 0·70 |
| 3 | 23·2 | 3 | 24·8 | 15 | 0·10 |
| 4 | 19·7 | 4 | 15·4 | 16 | 0·20 |
| 5 | 20·4 | 5 | 20·7 | 17 | 0·00 |
| 6 | 24·4 | 6 | 22·2 | 18 | 0·40 |
| 7 | 23·3 | 7 | 23·5 | 19 | 0·00 |
| 8 | 21·7 | 8 | 19·8 | | |
| 9 | 24·6 | 9 | 18·5 | | |
| 10 | 19·5 | 10 | 24·7 | | |
| 11 | 20·2 | 11 | 21·3 | | |
| 12 | 21·4 | 12 | 19·0 | | |
| Mean | 20·99 ±2·12 | | 20·78 ±3·85 | | 0·20 |

tion in many human physiological and pathological conditions.

Since acetylation is closely related to the metabolic processes leading to the formation and transfer of "active acetate," we investigated acetylation in 12 healthy people and in 19 patients with diabetes mellitus, of whom 7 were in diabetic coma. The technique used for the acetylation in vitro of sulphanilamide by the whole blood was the same as Blondheim's, 0·2 ml. of 3·6 mM sulphanilamide being added to 5 ml. of whole heparinised blood and incubated at 37°C for twenty-four hours. The results are shown in the accompanying table.

These results indicate that, whereas in diabetes mellitus acetylation does not differ appreciably from acetylation in healthy people, in diabetic coma it is completely absent.

REFERENCE

Blondheim, S. H. (1955) *Arch. Biochem. Biophys.* **55**, 365.

# New Inventions

## SCISSORS FOR POSTEROMEDIAL COMMISSUROTOMY IN MITRAL STENOSIS

DIGITAL splitting of the mitral valve is often impossible, because of the toughness or excessive mobility of the valve; and a variety of instruments—valvulotomes, guillotines, fingernail knives, dilators, and so on—have been devised for combined digital and instrumental commissurotomy. In a series of 270 patients with mitral stenosis we had to use instruments in 35% of cases; the corresponding figures reported by other workers range from 15 to 60%, and Sir Russell Brock tells us that he uses the valvulotome in 80% of his operations.

Splitting or cutting of the valve outside the line of the commissures, or damage to the chordæ tendineæ, may cause serious mitral regurgitation.

All the existing instruments have disadvantages.

With commissurotomes of the guillotine type bleeding is hard to control, and the operation must therefore be hurried. It is difficult to align the cutting edge of the instrument accurately with the commissure, which cannot be felt with the guiding finger at the moment of cutting. These disadvantages are shared by all the knife-like valvulotomes.

For all practical purposes the dilators and the cutting punch must be discarded.

The commissurotome of Nuñez is dangerous because it may tear the circumflex branch of the left coronary artery, and, if too much force is used, lacerate the heart wall.

When the right index finger is fitted with a fingernail knife of any type, then the tip of the right index finger cannot be used for splitting the postero-medial commissure of the mitral valve.

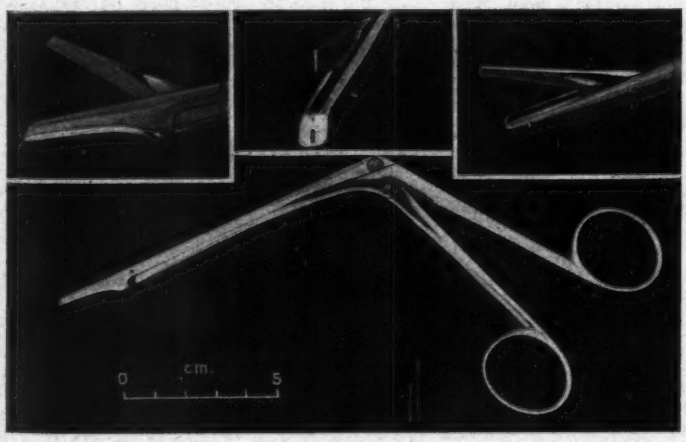



Fig. 1.

Struycken's conchotome, used for the surgical removal of the turbinate bones, was used for posteromedial commissurotomy in a new technique developed by A. G. Brom, director of this department. This new technique of inserting the instrument through a separate tiny incision was developed in view of the difficulty encountered in pronating the index finger when it was already in the heart, to the position where it could satisfactorily split the posteromedial commissure. The conchotome was later modified by Brom and Romanos by providing the moving jaw with a cutting edge and by covering the slit

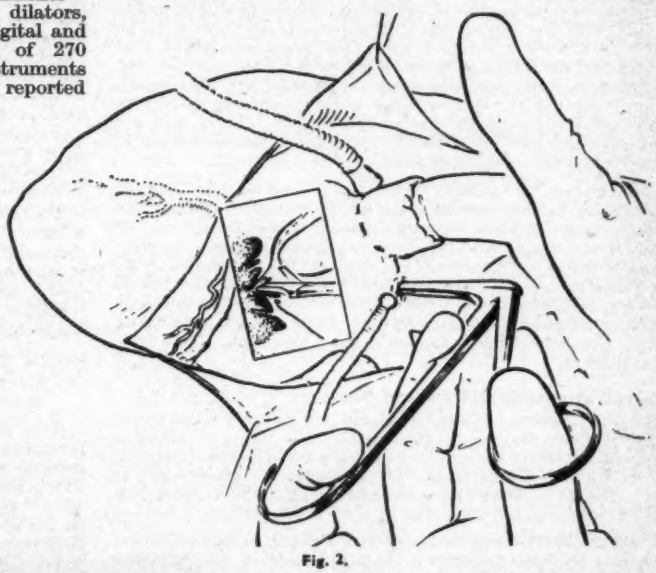


Fig. 2.

in the back of the fixed jaw with a fine strip of metal to prevent fragments of cut tissue from entering the blood-stream (fig. 1). The serrated edges of the fixed jaw were left. The instrument (which is kept closed during insertion and withdrawal) is introduced through a small incision in the wall of the left atrium, and the wall is closed over the instrument by a purse-string suture and a Rümel-Belmont tourniquet. The right index finger, introduced through an incision in the wall of the auricular appendage, guides the jaws under the posteromedial commissure (fig. 2), the jaws are opened and the commissure cut for a distance of 3–5 mm. This incision is lengthened if necessary, or the opening in the valve is widened by digital pressure. The instrument is withdrawn, and the atrial wall sutured in the usual way.

The conchotome is easily modified, and it ensures accurate valvulotomy without endangering other structures. As its slim shaft needs only a small incision in the atrial wall, little blood is lost during the operation, which need not be hurried.

Department of Thoracic Surgery, Academisch Ziekenhuis, Leiden, Holland

A. N. ROMANOS M.D.
F. E. DEROM M.D.

# Reviews of Books

## An Illustrated History of Science

F. SHERWOOD TAYLOR, M.A., PH.D. Illustrated by A. R. THOMSON, B.A. London: Heinemann. 1955. Pp. 178. 25*s*.

THIS handsome book, based on six Christmas lectures given in 1952 at the Royal Institution, amounts to a brief history of science written around the theme of its historical experiments, which were demonstrated at the lectures in a fashion as near as possible to that of their originators.

Half of the 120 plates are modern full-page drawings replacing the experiments, thus helping the text by revealing the background and personalities. They are admirably done, often with wit, and great care has been taken over detail, the sources of which are listed in an appendix. For example, the plate of William Harvey preparing to dissect obviously reproduces the operation table from Vesalius's *Fabrica*, the instruments being shown in disarray. Readers will probably start with the feeling that anachronisms are bound to be present: we did not find any. The lamp swinging in the cathedral at Pisa was quite different from the one we had always pictured when reading of Galileo, but the artist's note reads: "The scene is conjectural: the lamp similar to, but not identical with that shown at Pisa, but in fact not placed there until after Galileo's death." The portraiture in the pictures is remarkably good.

The roots of science pass down beyond the deepest strata of history into the darkness which surrounds the beginning of man himself. Somewhere round about 4000 B.C. some communities organised themselves into larger units. From then on science has developed with civilisation at an ever increasing speed, and the whole sweep of this development is here presented in a remarkable concise and readable survey. The book is a triumph for Dr. Sherwood Taylor, Mr. Thomson, and the publishers.

## Local Analgesia: Head and Neck

Sir ROBERT MACINTOSH, D.M., F.R.C.S.E., F.F.A. R.C.S., Nuffield professor of anæsthetics, University of Oxford; MARY OSTLERE, M.B.C.P.E., F.F.A. R.C.S., research assistant, Nuffield Department of Anæsthetics, University of Oxford. Edinburgh and London: E. & S. Livingstone. 1955. Pp. 138. 27*s*. 6*d*.

Sir Robert Macintosh and the Oxford school of anæsthetics have established a tradition in their presentation of practical and liberally illustrated monographs on local analgesia. The anatomy and the techniques of nerve injection are succinctly described, with the help of many clear and objective pictures, each of which tells so much more than text ever can. This latest work in a memorable line contains 145 original illustrations, all bearing the stamp of close acquaintance with the problems encountered in this type of work.

## Practice of Dynamic Psychiatry

JULES H. MASSERMAN, M.D., professor of neurology and psychiatry, North-Western University, Chicago. Philadelphia and London: W. B. Saunders. 1955. Pp. 790. 84*s*.

THE disorganised state of dynamic psychiatry, and the ebullient vitality of its proponents in the United States, are profusely shown in this textbook. Everything that came into Dr. Masserman's head as he was writing seems to have been thrown into the flowing stream of words, and his likes and dislikes are vigorously stated; he ranges from principles of psychiatric examination to "drug narcosis" and "biodynamics and social issues"; he offers a bibliography of about fifteen hundred items; and, inevitably amid this welter, there are many minor errors of fact and spelling. Dr. Masserman is, however, a widely read, experienced, and scientifically active psychiatrist who is not committed to adherence to any of the sects which sometimes further, and sometimes mutilate, dynamic psychiatry as it is practised in the United States. His approach to the whole controversial field is therefore broad and stimulating (except to the readers who demand precision of thought and language), his practical guidance is shrewd, and he is robustly critical of all rigid forms of psychotherapy, including traditional psycho-analysis. The book is in five parts, dealing in turn with methods of psychiatric examination, syndromes, case-studies and reports, psychopathology, and the practice of psychotherapy: this last section occupies more than half of the book. There are appendices on rather diverse topics, such as nomenclature of mental disorders, alcoholism, and the training of the psychiatrist. This large textbook is a refreshing variant on the usual tedious and dutiful statement of psycho-analytically-oriented or dynamic psychiatry.

## Pulmonary Resection for Tuberculosis

POUL OTTOSEN. Aarhus: Universitetsforlaget. 1955. Pp. 166. 21 Danish. Kr.

THIS attempt to evaluate lung resection in the treatment of pulmonary tuberculosis is based on the author's work first in the United States and later in Denmark.

After a historical review and recapitulation of the results in previously published series, he analyses two main groups. The first consists of 138 cases operated on in the Missouri State Sanatorium; the operations were undertaken for comparatively advanced disease and the results make an interesting comparison with the second, more recent, series of 43 patients operated on in Aarhus. More limited resections were possible in the second series and the results naturally more gratifying. The complications of the operation are dealt with in detail. There are some short case-records with well-produced radiographs that are interesting to consider in conjunction with the main text.

The work thus affords a useful critique of resection as a form of treatment, but it does not get to grips with the more difficult problem of deciding whether the operation is preferable to other forms of treatment in a particular case. Admittedly the author is not entirely wedded to resection as a means of surgical treatment, but it is clear he prefers it to collapse measures.

## Doctor in the Whips Room

Sir HENRY MORRIS-JONES, M.C., L.R.C.S.E. London: Robert Hale. 1955. Pp. 211. 18*s*.

THE author's adventures began early: he delivered a woman before he started to learn obstetrics; he was present in France at the execution of a deserter; in the front line his ability to speak Welsh saved him from arrest as an enemy. These and other stories are told in an autobiography revealing a first-rate and highly successful general practitioner, even if he was once duped by a confidence trickster. The second half of the book deals with his political life. There is Maxton's brilliant speech on the occasion of the golden wedding of the speaker; the sad farewell of J. H. Thomas to the House; and a grim visit to Buchenwald.

---

**Mental Health and Infant Development.**—The proceedings of the international seminar held by the World Federation for Mental Health at Chichester in the summer of 1952 have now been published in two volumes under the editorship of Dr. Kenneth Soddy. The first volume contains the lectures and summaries of the discussions held at the seminar. The second volume gives a representative sample of the case-histories of living French, British, and American children, which were distributed to members of the seminar as preparatory material. The British cases were prepared under the direction of Prof. D. R. MacCalman. (London: Routledge & Kegan Paul. 1955. Pp. 308 and 289. 25*s*. per vol.)

**The Medical Annual** (Bristol: John Wright & Sons. 1955. Pp. 548. 32*s*. 6*d*.).—The editors, Sir Henry Tidy and Prof. R. Milnes Walker, continue their notable service of providing a yearly review of progress. This year Dr. R. Bodley Scott has undertaken the section on blood diseases; and Dr. Kenneth Cameron has contributed a new section on psychiatry in childhood.

**Spot Diagnosis** (vol 2. London: Harvey & Blythe. 1955. Pp. 127. 8*s*. 6*d*.).—The Editors of *Medicine Illustrated* have prepared another collection of their entertaining puzzles. Some of the conditions illustrated are rare, but the devotees of this game will be ready for anything.

# THE LANCET

*LONDON: SATURDAY, DEC. 3, 1955*


## Formation of Urinary Stones

MANY of us still think in terms of urate, oxalate, or phosphate stones, for we were brought up that way; but recent investigations have shown that such a simple faith is misleading. A renal stone composed of one compound in pure or almost pure state is unusual. The chemical analysis to which we have been accustomed is crude and inaccurate; but by applying modern physical methods of analysis BARCLAY et al.[1] were able to show the prevalence of apatite (a complex of calcium and phosphate containing carbonate and hydroxyl groups) in 30 renal calculi submitted to X-ray crystallography. PRIEN and FRONDEL[2] classified 600 urinary calculi after examination by both X-ray and optical crystallography and found only 217 (36%) pure oxalate stones, in the mono- or di-hydrate forms (whewellite and weddelite) either singly or mixed. Uric acid was present in pure state in 30 stones, and mixed with oxalate and apatite in 7; so only 6% of stones contained urates. This is a lower proportion than might be expected from chemical analysis, in which the test for ammonium urate may be misleading.[3] 18 (3%) stones were pure cystine and 1 pure brushite; the rest were a mixture of oxalate and apatite, struvite and apatite, or the three compounds together.

A knowledge of the true composition of stones carries us little further towards the cause of their formation; but it does suggest means whereby they may be prevented or dissolved. Since calcium is the prevalent cation in 90% of all urinary calculi, it is reasonable to infer that its physico-chemical properties can be controlled so that its salts are prevented from crystallising from the urine. There is the school of "passivists" who hold that stones will not form in normal urine. PRIEN and WALKER,[4] for example, think that by certain means the calcium salts are kept in solution and that this mechanism should be protected and sustained. According to this view, urinary glucuronosides provide stabilising compounds with calcium ions, and they are destroyed or inactivated by infection, thus leading to stone. Since 25% of a dose of sodium salicylate taken by mouth is excreted in the urine as glucuronosides, PRIEN and WALKER gave this drug to 19 patients with recurrent stones, and encouraging results were recorded in 17. In 6 other patients with indwelling catheters encrusted by calculi, administration of salicylate prevented the formation of these concretions. The "activists," on the other hand, work from the premise that the urine contains substances, either normal or abnormal constituents, which steal the calcium cation from solution. The colloid matrix of the stone is often incriminated. BOYCE et al.[5] noted two mucoproteins in normal urine which retained a negative charge throughout the whole range of urinary pH; they found that these mucoproteins were much increased in calculous disease and particularly in hyperparathyroidism. "Uromucoid" was the name given to these substances. The same workers[6] have now considered the possibility of "micelle" formation. Mucoproteins in urine contain chelate rings with which calcium may be leached out of inorganic solution on to the protein moiety. Thus calcium chelates may be formed in a colloid micelle which can be disturbed by shifts of pH and alterations of inorganic environment, so that crystalline calcium compounds are precipitated from the micelle—rather as water is squeezed out of a sponge. BOYCE et al. admit that uromucoid would act in this way as a detergent in urine only if it was modified so that both carboxyl and amino groups could be freed. Their suggestions are supported by the fact that the process can work in reverse, and stones may be dissolved in vitro by chelating agents such as ethylenediamine tetra-acetic acid,[7] which has been used by GEHRES and RAYMOND as an irrigating solution in the bladder and kidney for this purpose.[8] In 1 patient out of 7 complete dissolution of a bladder stone was achieved. SUBY et al.[9] attempted renal irrigation in 2 patients but treatment was stopped because of pain; the pH of their solution was 4·5 and 'Tween' had been added. GEHRES and RAYMOND used a 1% solution at pH 7·3 and reported no disturbing symptoms. It is interesting to note that RAINS has been investigating micelle mechanisms in the formation of biliary calculi.[10]

The factors which may prevent stones forming, or dissolve them after they have formed, do not necessarily indicate the causes of stone formation: the mechanisms need not be the same and this confusion has often arisen in the past. It would be wrong to suppose that because calcium salts may be prevented in one way or another from coming out of solution and because stone formation is thus avoided, stones are therefore formed by a reversal of that process. A mechanistic hypothesis has been put forward by CARR.[11] His work is founded on RANDALL'S[12] observation of calculous plaques at the apex of renal papillæ; calcium deposits were found in this situation in 17% of 429 pairs of kidneys examined at necropsy. He also found 28 renal calculi adherent to and apparently growing upon renal papillæ. ANDERSON and MCDONALD[13] studied RANDALL'S plaques more closely and found them to be an accumulation of calcareous particles which were apparently formed by phagocytic ingestion; their situation in the renal papilla could then be explained by the fact that calcium is reabsorbed in the tubules, and may be in such concentration as to become particulate and require phagocytic mobilisation. Whereas RANDALL and ANDERSON used histo-

1. Barclay, J. A., Cooke, W. T., Stacey, M. *J. Physiol.* 1944, **103**, 24.
2. Prien, E. L., Frondel, C. *J. Urol.* 1947, **57**, 948.
3. Higgins, C. C. Renal Lithiasis. Springfield, Ill., 1943; p. 53.
4. Prien, E. L., Walker, B. S. *New Engl. J. Med.* 1955, **253**, 446.
5. Boyce, W. H., Garvey, F. K., Norfleet, C. M. *J. Urol.* 1954, **72**, 1019.
6. Boyce, W. H., Garvey, F. K., Norfleet, C. M. *Amer. J. Med.* 1955, **19**, 87.
7. Kissen, B., Natelson, S. *Science*, 1950, **112**, 367. Raymond, S., Gehres, R. F. *Proc. Soc. exp. Biol., N.Y.* 1950, **74**, 715. Abeshouse, B. S., Weinberg, T. *J. Urol.* 1951, **65**, 316.
8. Gehres, R. F., Raymond, S. *J. Urol.* 1951, **65**, 474.
9. Suby, H. I., Albright, F., Wayne, J., Dempsey, E. *Ibid*, 1951, **66**, 527.
10. Rains, A. J. H., Crawford, N. *Nature, Lond.* 1954, **191**, 829. Rains, A. J. H. *Gastroenterologia, Basel*, 1955, **83**, 18.
11. Carr, R. J. *Brit. J. Urol.* 1954, **26**, 105; see *Lancet*, 1954, ii, 1009.
12. Randall, A. *Ann. Surg.* 1937, **105**, 1009.
13. Anderson, L., McDonald, J. R. *Surg. Gynec. Obstet.* 1946, **82**, 276.

logical techniques, CARR studied these deposits by direct X-ray photographs of the exposed kidney at operation and also by preparing autoradiographs from thin slices of 98 kidneys removed by operation and 111 obtained at necropsy. A normal kidney contains one, two, or more opacities just visible to the naked eye. Sometimes they are larger and composed of many small concretions which have accumulated together, often in lines. In the presence of calyceal stones renal concretions are more abundant than usual, and they are often situated in the area draining into the corresponding calyx. CARR also found that the concretions were just outside the fornices, in line with but outside arteries and veins. Here the renal lymphatics pass out into the renal sinus; and CARR has therefore suggested that the concretions are lying within the lymphatics and that this is a normal method of removing particulate matter from the kidney and its pelvis. Should a lymphatic become obstructed, concretions may accumulate at the fornix and break through its thin endothelial sheath into the calyx, whereupon a stone may grow from deposition of urinary salts around the concretions. Further back in the lymphatic more concretions come to rest in linear deposition, and the damming-back process may go so far as the renal papilla—hence RANDALL's plaques.

Most, if not all, the known ætiological factors in stone formation would fit into CARR's hypothesis: the lymphatic-drainage mechanism would tend to break down from overloading with microliths because of disturbed calcium metabolism, or a failure of colloidal solution: alternatively inflammation would obstruct lymphatics by fibrosis. The tendency to recurrence [14] after removal of a stone becomes understandable; indeed CARR suggests that the appropriate renal segment or lobule should be excised with the removal of a calyceal stone. Furthermore, he has identified the composition of concretions with that of stones described by PRIEN and FRONDEL.[2] Finally, if renal concretions lie within the lymphatics, which drain outside the kidney, certain extrarenal concretions might have the same X-ray diffraction patterns as intrarenal concretions and frank stones; and CARR has shown that they have.

## Nutrition and Vitamin $B_{12}$

WE know vitamin $B_{12}$ as the factor necessary for the proper development of the red blood-cells: when it is not absorbed a megaloblastic anæmia ensues, with typical changes in the bone-marrow. Vitamin $B_{12}$ is derived from food, and it is absorbed from the alimentary tract only in the presence of the intrinsic factor (hæmopoietin) secreted by the stomach. Pernicious anæmia, the archetype of megaloblastic anæmias, develops because the stomach ceases to secrete the intrinsic factor and therefore the 1 μg. or so of vitamin $B_{12}$ that a man needs daily is not transported across the intestinal mucous membrane—a striking example of starvation in the midst of plenty. We now know of other megaloblastic anæmias due to deficiency of vitamin $B_{12}$. The megaloblastic anæmia after total gastrectomy is not hard to understand, since the area of gastric mucosa that secretes intrinsic factor is removed; CALLENDER et al.[15] have shown that intrinsic-factor secretion and vitamin-$B_{12}$ absorption are in fact greatly reduced in these patients, and WATSON and FLOREY [16] produced the same sort of result with experimental gastrectomy in rats. What is surprising is that it is two or three years before the anæmia appears after gastrectomy, suggesting that the body possesses a considerable store, perhaps 1000–2000 μg., of vitamin $B_{12}$. PITNEY and BEARD [17] followed the serum level of vitamin $B_{12}$ in a patient who had had a total gastrectomy for carcinoma of the stomach; the level fell slowly and did not fall below the normal minimum of 86 μμg. per ml. until eight months had passed. After nineteen months the serum-$B_{12}$ was below 50 μμg. per ml.; which is the upper limit in patients with pernicious anæmia (the average level in pernicious anæmia is about 13 μμg. per ml.); but in spite of this further fall the gastrectomy patient still had no megaloblastic anæmia.

A megaloblastic anæmia in which nutrition plays at least some part is that reported by FOY and his co-workers in East Africa. In their latest paper [18] they show that the patients who respond to treatment either with penicillin or with relatively small doses (80 μg.) of vitamin $B_{12}$ by mouth have low serum levels (20–100 μμg. per ml.) of vitamin $B_{12}$. The diet of these people is poor in animal protein and rich in bulky carbohydrates. It may be actually deficient in vitamin $B_{12}$, and it is likely that this type of diet encourages the growth in the intestine of organisms that successfully compete for the available vitamin $B_{12}$, leaving little for absorption; and these organisms are presumably sensitive to penicillin. There is good evidence that in these patients gastric function is usually unimpaired.

In food vitamin $B_{12}$ is usually associated with animal protein; it has been detected in only one or two vegetable foods, such as groundnuts. Vegetarians, even in temperate climates, might therefore be short of vitamin $B_{12}$, and, if a purely dietary deficiency ever occurs, it is among vegetarians that the evidence might be found. WOKES et al.[19] have investigated this matter. They appreciate the fact that the ordinary British vegetarian does, in fact, consume quite a lot of animal protein in the form of milk, butter, cheese, and other dairy products. The proportion of total dietary calories he gets from animal protein is just under 3%, whereas in the average non-vegetarian diet in the United Kingdom the figure is about 6%. The British vegetarian gets as much animal protein in his diet as the ordinary Greek or Italian, and much more than most people in India, for instance. But there are some vegetarians (vegans) who have entirely eliminated dairy products from their food and eat no animal protein at all; and groundnuts are also absent from their diets. As might be expected, symptoms of deficiency do not become noticeable until they have kept to the vegan diet for some years, and some of them seem to escape definite symptoms even after five years on the diet. The commonest and earliest symptoms are in the mouth; sore tongue is often prominent. Of the 32 British vegans studied

14. Pyrah, L. H. *Brit. med. J.* 1954, ii, 963.
15. Callender, S., Turnbull, A., Wakisaka, G. *Clin. Sci.* 1954, **13**, 221.
16. Watson, G. M., Florey, H. W. *Brit. J. exp. Path.* 1955, **36**, 479.
17. Pitney, W. R., Beard, M. F. *Arch. intern. Med.* 1955, **95**, 591.
18. Foy, H., Kondi, A., Manson-Bahr, P. E. C. *Lancet*, Oct. 1, 1955, p. 693.
19. Wokes, F., Badenoch, J., Sinclair, H. M. *Amer. J. clin. Nutr.* 1955, **3**, 375.

by WOKES et al., 27% had oral symptoms. Paræsthesiæ developed in 20%. Amenorrhœa or other menstrual disturbances occurred in 8 of the 22 women aged between fifteen and forty-five years. The menstrual symptoms appeared early; for example, after four years on the vegan diet paræsthesiæ were present in 4%, oral symptoms in 6%, but menstrual symptoms in 24%. Nervous symptoms were also common and about 20% complained of pains in the back and spine. WOKES et al. estimated the serum-$B_{12}$ level in some of the vegans. The normal is 200–320 μμg. per ml. and in the vegans the levels varied from 45 to 193 μμg. per ml.; 9 had levels of less than 100 μμg. per ml. and were considered to be definitely deficient in vitamin $B_{12}$, but all these 9 had been on vegan diet for at least six years. Hæmoglobin levels were normal, but, in some, red-cell counts were a little low and the mean corpuscular volume a little high. One of the vegans, a boy of 15 who was deficient in vitamin $B_{12}$, did develop typical subacute combined degeneration of the spinal cord and details of this case have been described by BADENOCH.[20] This patient responded very well to treatment with vitamin $B_{12}$ alone. WOKES et al. point out that vegetables contain comparatively large amounts of folic acid; and, since folic acid is known to precipitate the onset of neurological symptoms in classical pernicious anæmia, it is conceivable that the folic acid in the diet may have a similar effect in vegans who have become really deficient in vitamin $B_{12}$.

For comparison with the British vegans, some information is available about Dutch [21] and American [22] groups. Both seem to be less affected than the British vegans; no deficiency symptoms were observed in 26 American vegans who had been on a diet free from animal protein for five years or more. The Dutch group had symptoms like those of the British vegans, but less commonly. WOKES et al. point out that the Dutch group had been on vegan diets for an average of only two years, compared with five or six years in the British group. The British vegans had the lowest protein intake; the Americans obtained 10·4% of their calories from protein, the Dutch 9%, and the British only 7%. This difference may be correlated with the observation that animals on a diet free from animal protein have a poor rate of growth and development which can be corrected by giving them vitamin $B_{12}$, but only if the diet is adequate in total protein. Possibly the British vegans could at least postpone their symptoms by increasing their intake of non-animal protein.

There is still controversy about whether the addition of vitamin $B_{12}$ to the diet in small quantities (10 μg. daily) by mouth has any effect on the growth and development of children. American claims that such a supplement accelerated the growth of undernourished children could not be substantiated elsewhere.[23] WOKES et al. state that the growth and development of British vegetarian boys showed no significant abnormalities, but these workers have little information about children on the restricted vegan diets. It is known that vegan children have been successfully reared, though they are often breast-fed for longer than usual; and symptoms of vitamin-$B_{12}$ deficiency were commoner in the children than the adults. There is certainly no support in these studies for the general use of vitamin-$B_{12}$ supplements for children.

20. Badenoch, J. *Proc. R. Soc. Med.* 1954, **47**, 426.
21. Donath, W. F., Fischer, I. A., Meulen van Eysbergen, H. C. van der, de Wijn, J. F. *Voeding*, 1953, **14**, 153.
22. Hardinge, M. G., Stare, F. J. *J. clin. Nutr.* 1954, **2**, 73.
23. See *Lancet*, 1952, ii, 1165.

## Experiments in Liaison

THE National Health Service Act of 1946, which changed the whole structure of the health service of the country, did nothing, initially, at least, to break down the barriers that separated the three branches of the profession. Not all the blame for this however, can be laid on the Act; the profession itself must take its share. There is no doubt that some of the provisions of the Act appeared—directly or indirectly—to make many of the barriers more formidable than they were, or to raise new ones. There was, for example, the removal of the municipal hospital, the chest clinic, and the mass-radiography unit from local-authority control. The widening of the responsibility of the health visitor also had important repercussions, which affected in many ways the local authority's relations with general practitioners and hospitals. The Children Act, 1948, which created new departments and new staff (usually separate from the public-health department), produced further problems. But these obstacles are in reality flimsy and unstable; for most of them rest on shallow foundations of prejudice and misunderstanding which can be broken by unity of purpose and joint effort.

In liaison between the public-health department, the family doctor, and the hospital staff, there has been gradual but accelerating improvement, though there are big differences throughout the country. That this improvement could be carried further is evident from the frequency with which the words "coöperation" and "liaison" are used in Ministerial speeches, official circulars, and articles in the medical and lay press. The subjects of problem families and the welfare of children in their own homes, the need for a proper domiciliary team and the rôle of the health visitor, and the control of tuberculosis have been recent contexts for these remarks. But strenuous efforts have been and are being made to knit the work of the family doctor and the municipal health services more closely together. In Birmingham [1] general practitioners were offered the use of clinic premises; THOMAS [2] has urged his fellow practitioners to seize the chance of the help which the health visitor can provide; and CHALKE [3] and others have described schemes which aim at bringing this about. The Minister of Health, addressing the Executive Councils Association, has advocated more part-time hospital appointments for general practitioners; and he welcomed the action of the British Medical Association in asking local medical committees to make plans with medical officers of health to ensure that general practitioners could play a part in preventing the break-up of families.[4] In some respects the bonds between hospital and local authority have been tightened since 1948, largely as a result of regular visits by health visitors and clinic doctors to special departments—pædiatric, diabetic, asthma, psychiatric, geriatric, and physical medicine. In the care of diabetics, for

1. Annual Report for 1952, Medical Officer of Health, Birmingham.
2. Thomas, J. J. S. *Brit. med. J.* 1953, ii, 964.
3. Chalke, H. D. *J. R. Soc. Hlth.* 1955, **8**, 605.
4. *Lancet*, Oct. 29, 1955, p. 932.

instance, special health visitors were used in Cardiff as long ago as 1944 [5]; and an extension of this work elsewhere has given good results.[6] Better coördination of effort is conspicuously needed too in tackling the growing problems of the aged; and here the local health authority has big responsibilities. The Rutherglen experiment [7] is an example of what good team-work can do; and the seconding of health visitors to work in association with geriatric units has been tried in a number of hospitals with great success.[8] A number of surveys and inquiries have also demonstrated the value of the combined operation: we recall the ones concerned with tuberculin testing and mass radiography in the Rhondda Fach [9] and tuberculosis in Blyth.[10] As for tuberculosis control, we observed a few weeks ago [11] that the division of command may hamper the preventive approach, and that the expanding work of the epidemiologists could be better coördinated. An illustration of the way in which good human relations can be established within the health service may be found in the account, by Dr. STEPHEN TAYLOR and his colleagues,[12] of the Harlow health centres, which they term "an essay in coöperation." Nearly all general practice in the new town will be conducted from the health centres, "in day-to-day association" with the clinics of the local health authority.

DAVID MORRIS [13] believes that it is in the care of children that the work of the three authorities comes closest together. (Each child, he reminds us, has at least three doctors, who may work independently of each other.) He and his associates decided that the pædiatric outpatient department was a good place for an experiment in working coöperation with the local authority. The health visitors in the area were in turn seconded to the department by rota. The visitor in attendance passed on information to the clinic and the health visitor concerned, after a consultation with the almoner. It has been good to see how well health visitors and almoners are now working together, and this is borne out by the almoner, quoted by MORRIS, who found the experiment "wholly advantageous." She pointed to the different situations of the almoner and the health visitor; the former is generally concerned with a patient in an emergency, while the latter has a less urgent duty; and by dovetailing the knowledge of both the patient is likely to receive more constructive help. Under the new arrangement the health visitor also saves the time of the pædiatrician by advising on such matters as mixed feeding; and this is advice which, in any case, is probably given more effectively by the health visitor. All the children attending this outpatient department are referred by their general practitioners, who are kept informed of what is being done. Seminars on topics of child health are arranged at the hospital, to which both health visitors and practitioners are invited.

It is by constructive efforts such as these that the obstacles to a really united health service will be removed. The deliberations of liaison committees and the advice of official circulars can give useful help; but the success of the National Health Service depends in the end not on committees and circulars but on the spirit of those who do its everyday work. We welcome these signs that this spirit is becoming more original and adventurous.

5. Wilson, J. G. *Mon. Bull. Minist. Hlth, Lab. Serv.* 1951, **10**, 204.
6. Walker, J. B. *Lancet*, 1953, ii, 445; *Brit. med. J.* July 30, 1955, p. 317.
7. Anderson, W. F., Cowan, N. R. *Lancet*, July 30, 1955, p. 239.
8. Andrews, C. T., Wilson, T. S. *Ibid*, 1953, i, 785.
9. Cochrane, A. L., Cox, J. G., Jarman, T. F. *Brit. med. J.* 1952, ii, 843.
10. See *Lancet*, Oct. 29, 1955, p. 921.
11. *Ibid*, Oct. 22, 1955, p. 857.
12. *Ibid*, p. 863.
13. Morris, D. *Woman Hlth Offr*, 1955, **9**, 283.

## Annotations

### HEROIN

ADDICTION to heroin can be a dreadful disease, and in some countries it is widespread. Among possible means of preventing it, the withdrawal of heroin from medical practice has been under discussion internationally since 1923. Whether much would in fact be gained by stopping all medical supplies has often been questioned, because anyone who has some morphine and a laboratory can turn it into heroin overnight. Nevertheless, after all these years of discussion, the World Health Organisation is now persuaded that this action is necessary. A ban would not only remove medical opportunities for acquiring addiction but would considerably simplify the detection and conviction of traffickers, since, where a drug is illicit, its mere possession becomes a clue. In this difficult campaign the United Nations needs the moral support of all the principal countries, whether or not they have a heroin problem: and it would not be helped substantially if Britain merely prohibited export of what she manufactures.

Believing firmly in the need for international action in medicine as elsewhere, we have already expressed our own opinion [1] that the Government were right in telling the United Nations that we shall do what they ask; and this week we publish, on p. 1183, a review of the subject which, though brief, may offset some impressions left by even briefer letters in the newspapers. We agree, however, that difficult issues are raised by the Government's decision, and that some of the objections lately put forward are both sincere and reasonable. It is said, for example, that the Standing Medical Advisory Committee of the Central Health Services Council were not entitled to speak for the profession on so important a matter as the banning of a drug (something never done before); and this argument will be conclusive for those whose idea of democracy is limited to majorities and specific mandates. It is less convincing, however, to those who think that excess of democratic methods can be fatal to democracy, and are content, for certain purposes, with indirect representation by a body of respected people who are told to use their own judgment. Looking at the constitution of this particular committee,[2] we should ourselves think them as likely as anybody—or as any other body—to give a sound and dispassionate answer to the first question they were asked "Is heroin indispensable?" Moreover, their answer "No" was surely the only possible answer in view of the facts (1) that the British Pharmacopœia Commission, with the authority of the General Medical Council, had in 1952 removed this drug from the pharmacopœia, and (2) that a great number of doctors, of all degrees of eminence, long ago dispensed with it in their practice. On the further implied question whether—primarily to help in the control of drug-addiction abroad

1. *Lancet*, 1955, i, 1311.
2. The members last December were: Sir HENRY COHEN, F.R.C.P.; Dr. JANET AITKEN; Sir RUSSELL BRAIN, F.R.C.P.; Dr. J. A. BROWN; Dr. C. METCALFE BROWN; Sir DAVID CAMPBELL, F.R.F.P.S.; Sir ERNEST ROCK CARLING, F.R.C.S.; Prof. DIGBY CHAMBERLAIN, F.R.C.S.; Prof. ROBERT CRUICKSHANK, F.R.C.P.; Mr. O. M. DUTHIE, F.R.C.S.; Sir ARTHUR GEMMELL, F.R.C.O.G.; Dr. E. A. GREGG; Dr. W. V. HOWELLS, Prof. A. J. LEWIS, F.R.C.P.; Dr. W. G. MASEFIELD; Sir HARRY PLATT, F.R.C.S.; Dr. F. M. ROSE; Sir JAMES PATERSON ROSS, F.R.C.S., Dr. J. G. SCADDING; Dr. W. P. H. SHELDON; and Dr. C. W. WALKER.

—Britain should agree to the United Nations' request, the committee's answer could not be a statement of fact: it could be no more than an opinion. Undoubtedly, the Royal Colleges, the British Medical Association, or the whole profession through a plebiscite, could in the same way have expressed an opinion; but, whatever doctors might have said, their rôle would still have been limited to advice; for the only people finally entitled to decide are the electorate—who are also the patients. Fortunately in this country we do not yet attempt to refer such problems, every few weeks, to the millions of voters; so it is Her Majesty's Ministers, responsible to Parliament, who are now having to choose on their behalf between the World Health Organisation and the Fellowship for Freedom in Medicine.

If the Fellowship were right, and if the unprecedented decision to ban the use of a drug involved a real threat, by politicians and officials, to medical freedom, this would of course be the moment to rally the profession against the Government. But does it? As so often, we seem to be confronted by the conflicting claims of principle and common sense. On pure principle, no answer is possible to the argument that heroin must not be banned so long as there is a single doctor in Britain who wants to use it. But supposing 10% of our fellow citizens were heroin addicts, should we still, for this one doctor's sake, reject the ban? Probably not. In that case, on what conception of medical ethics can we regard our principle as inviolable when we are asked to help drug addicts abroad? Admittedly, the doctor personally undertakes to do his utmost for his patient, and to that end he ought to be free to use the method of treatment that he thinks will help the patient most. But there are often limits to what he can do—limits set, for instance, by the rationing of certain drugs, by lack of the right accommodation, or even by the ruling of judges who claim that professional confidence must not interfere with the course of justice. In undertaking to help his patient as much as he can, the doctor recognises, perforce, that the community also has its rights. And it has never been customary in medicine to suppose that the human community ends on the cliffs of Dover.

## COLOUR RADIOGRAPHY

BECAUSE of the short wave-length of X rays it is not of course possible to make a colour film directly. For exhibition purposes in the past, various colour radiographs have been made, either by colouring the negatives by brush with a special stain [1] or by superimposing three radiographs taken at high, medium, and low voltage through colour filters.[2]

Bryce [3] has now experimented with tricolour paper to obtain some direct colour. The negative film and printing paper of this type contain three emulsions; the top is sensitive to blue, the middle to blue and green, and the deepest layer to blue and red. A yellow filter is placed between the top and middle emulsions, allowing only green and red light to reach the deeper layers. At the end of development, a fix-bleach solution removes the yellow filter and the silver salts, leaving only the three dye images. Using this material and a front intensifying screen, it is possible to make a two-colour radiograph by exposing the emulsion to coloured light during development. The result is a radiograph with a brown image where there has been no exposure, and various shades of brown and green at intermediate levels.

If an emulsion could be produced which would allow a considerable variation in colour between areas of small X-ray opacity then this method would become more than a novelty. But it is unlikely that any of the known materials would be suitable.

1. Dowdy, A. H., Bonnan, L. J. *Amer. J. Roentgenol.* 1953, **70**, 581.
2. Donovan, G. E. *Lancet*, 1951, **i**, 832.
3. Bryce, A. *Brit. J. Radiol.* 1955, **28**, 552.

## DEPRIVED AND DELINQUENT CHILDREN

THE latest report [1] on the work of the Home Office Children's Department is on the whole an encouraging document. The expansion of the boarding-out system for deprived children has accorded with the findings of psychologists and sociologists on the one hand and with economic necessity on the other. We have known for a long time that large hostels and institutions are bad for the mental health of the child inmates, and that other ways, including boarding-out and fostering, are needed to afford children individual attention and affection. The relative costs cited in this report—£1 12*s.* per week per child in a foster-home and £6 4*s.* in local-authority homes and nurseries—show the extensive economies that can be effected by the present trend in official policy. Between 1949 and 1954 the proportion of children boarded out increased until some 44% were provided for in this more satisfactory way. The importance of obtaining an increased number of suitable foster-parents in order to sustain the present trend is realised by the Home Office. The time is clearly not far distant when foster-parents will be fully trained social workers in their own right—receiving, one should hope, a rather more liberal allowance for this public service. Also in the "family group homes" developed over recent years the aim has been to create a substitute family atmosphere for deprived children. Such homes, of six to twelve children under the control of a house-mother or a house-mother and house-father, are established in an ordinary neighbourhood so that the children can attend local schools, have their friends in to tea, and in every way live their lives as members of the community. By the end of 1954 there were some four hundred such family homes, and the indications are that they will be developed at an increasing rate.

Although the number of children and young people charged with offences has decreased in the past two years, the numbers found guilty of indictable offences still exceed the pre-war level. New methods of combating juvenile crime include an experimental scheme of juvenile liaison officers operated by the Liverpool police force. This scheme is devised to treat early delinquents and near-delinquents by means of cautioning and home visiting by special non-uniformed officers, with a view to stimulating parental control and preventing a child drifting unchecked into delinquency. While the falling figures in Liverpool cannot prove (any more than rising figures could disprove) the value of this scheme, the Home Office has considered its merits seriously and recommends its possible extension to other parts of the country.

A brief account of the first detention centre, established at Kidlington in 1952, is not heartening reading. Of the five hundred boys who had been discharged, after serving between three and six months under strict discipline and close supervision, three hundred were subject to a further court order, and of the remaining two hundred only twenty could be persuaded to accept a period of voluntary aftercare supervision. This suggests that tough treatment and short, sharp discipline are just as likely to increase resentment as to make hardened offenders more amenable. There is clearly no easy substitute for the patient, individual methods of borstal and approved school.

For research the Home Office has to rely heavily on the resources of the large trusts and a few university scholars. Obviously much more needs to be done in the way of evaluating new methods of treating both young offenders and deprived children if we are going to develop an efficient, flexible service.

1. Home Office: Seventh Report on the Work of the Children's Department. H.M. Stationery Office, 1955.

## THE HYPERSENSITIVE XIPHOID

IN view of the wide variations in size, position, and orientation of the xiphoid, it is surprising that so few symptoms can be related to disorders of this bone. Very occasionally a gross disturbance of shape or position causes epigastric pain, nausea, or vomiting. When there is such a malformation, and when the symptoms can be produced by local pressure, excision of the xiphoid brings relief. But such cases are rare, and more commonly pain referred to the xiphoid is associated with organic lesions in the chest or abdomen. In the absence of such lesions, the xiphoid itself may be responsible for symptoms which simulate those of coronary disease or peptic ulceration. If pressure upon the xiphoid reproduces the patient's symptoms, this association must be borne in mind. It is clear, however, that the xiphoid is often tender, both in normal people and in those with organic chest and abdominal disease, and the term xiphoidalgia, coined by Junghanns,[1] must be used with caution. Lipkin et al.[2] have investigated the hypersensitive xiphoid in a number of patients. They suggest that procaine infiltration, repeated when necessary, often abolishes the symptoms, and such a therapeutic test may be of diagnostic value.

## INFANTILE GASTRO-ENTERITIS

SEVERAL Continental workers [3–7] have lately written theses on the specific serological types of *Escherichia coli* and their association with epidemic infantile gastro-enteritis. A new monograph by Smith, of Aberdeen, now records some of the findings and views in this country.[8]

Bray [9] first demonstrated the importance of a specific serological type of *Esch. coli* in epidemic infantile gastro-enteritis, and much important work has followed, notably by Joan Taylor and Smith. It is fitting, therefore, that Smith should have written the first British monograph on this subject. He makes an excellent survey of the investigations, but those who have been studying these problems may wish that he had set out to write a longer book in which he could have analysed the work more fully, and discussed at greater length the arguments for and against these specific serological types of *Esch. coli* being the cause of infantile gastro-enteritis. He gives a clear summary of Kauffmann's serological classification, and a useful list of where and when each serological type has been found in epidemics of infantile gastro-enteritis. There is mention too of the work on the white scours of calves, a closely related disease caused by certain specific serological types of *Esch. coli*, some of which also cause enteritis in babies.

Smith's observations on the biochemical patterns of many strains of *Esch. coli* type O.111 anticipated the later identification of the different H types of that organism. He gives several references to show how the demonstration of these different H antigens has been used in epidemiological studies. One of his rare omissions is any reference to the work of the French investigators, headed by Nicholle,[10] who have shown that a similar subdivision of the types can be made by specific phages.

The best part of the monograph deals with the 1947 epidemic in Aberdeen, which was probably the most extensive that has been recorded since these specific serological types of *Esch. coli* were recognised, and in which there were 104 deaths amongst the 240 cases infected with *Esch. coli* types O.111 (B4) and O.55 (B5). Many of the points which have been stressed by later workers were fully examined in 1947 by Smith and his colleagues, Giles and Sangster: they showed how the younger babies, especially those in institutions, were most often affected, how the infants in the slums were infected outside hospital, how previous illness predisposed to enteritis, and how breast-feeding protected these babies. They also found that vomiting was an important early symptom (60% of 180 cases); that it was valuable to segregate the doubtful cases and that epidemics could be shortened by rapid segregation of carriers and cases: and that when an epidemic was being investigated it was important to examine the nurses as well as the babies.

1. Junghanns, H. *Zbl. Chir.* 1940, **67**, 628.
2. Lipkin, M., Fulton, L. A., Wolfson, E. A. *New Engl. J. Med.* 1955, **253**, 591.
3. Le Minor, S. *Nourrisson*, 1953, **41**, 209.
4. Braun, O. H. *Ergebn. inn. Med. Kinderheilk.* 1953, **4**, 52.
5. Grönroos, J. A. *Ann. Med. exp. Fenn.* 1954, **32**, suppl. no. 4.
6. Schmidt, E. F. *Beih. Arch. Kinderheilk.* 1954, **28**, 1.
7. Dupont, A. Epidemic Infantile Diarrhœa. Copenhagen, 1955.
8. Smith, J. The Ætiology of Epidemic Infantile Gastro-enteritis, Royal College of Physicians of Edinburgh Publications, 1955. no. 5.
9. Bray, J. *J. Path. Bact.* 1945, **57**, 239.
10. Nicholle, P., Le Minor, L., Buttinaux, R., Ducrest, P. *Bull. Acad. Med., Paris*, 1952, **136**, 483.

## ANTI-HISTAMINES AND ASTHMA

IT has been known since 1934 that a substance which is an anti-histamine precursor can cause contraction of smooth muscle [1]; and since the introduction of anti-histamines into clinical practice evidence has accumulated that in the doses used they can produce bronchoconstriction in asthmatics. Anti-histamines have been found to be relatively ineffective in the treatment of asthma; but it is only recently that it has been shown that they may sometimes make the condition worse.

Given by mouth some of these drugs reduce vital capacity in some asthmatics.[2 3] 'Antergan' and mepyramine inhaled as 2% aerosols cause transient bronchoconstriction in man [4]; and Herxheimer [5] found that asthmatic dyspnœa was invariably aggravated by inhalation of aerosols in concentrations greater than 1–3%, although lower concentrations gave some relief. Hawkins [6] has studied 12 well-known anti-histamines and found that they all cause bronchoconstriction in animals. He also confirmed the finding that mepyramine caused contraction of isolated human bronchial muscle [7] and concluded that "the bronchoconstrictor action of the antihistamine drugs tested may well be a factor limiting their therapeutic activity in asthma." It is known that some anti-histamine drugs may cause histamine release in the body,[8 9] and Hawkins suggests that this may be the cause of the bronchoconstriction, because the drug is not usually present in sufficient concentration to block the action of the histamine which it has itself caused to be released. Hawkins's explanation has as yet little practical evidence to support it, but since it is now clear that anti-histamines may cause bronchoconstriction in man it is reasonable to suggest that they should not be used routinely in asthmatics.

In chronic diseases such as asthma and parkinsonism, where there is a natural and proper tendency to try any drug that may help, that drug should be assessed critically and abandoned unless undoubted improvement has followed its use. But the multitude of synthetic drugs now available makes selection particularly difficult. At present there are at least 18 different anti-histamine compounds available under at least 37 names, not to mention various tablets containing mixtures of them. The clinical trials so far recorded suggest that 3 or 4 compounds at the most are all that need be used and that there is little to choose between most of these drugs from a medical standpoint. Goodman and Gilman [10] remark: "Perhaps in no other class of therapeutic agents does the physician enjoy a wider choice of preparation, but in no other group of drugs does a discerning choice offer less reward."

1. Bovet, D. *C.R. Soc. Biol. Paris*, 1934, **116**, 1020.
2. Levy, L., Seabury, J. H. *J. Allergy*, 1947, **18**, 244.
3. Criep, L. H., Aaron, T. H. *Ibid*, 1948, **19**, 215; *Ibid*, p. 304.
4. Charlier, R., Philippot, E. *Arch. int. Pharmacodyn*, 1949, **78**, 559.
5. Herxheimer, H. G. T. Management of Bronchial Asthma. London, 1952; p. 56.
6. Hawkins, D. F. *Brit. J. Pharmacol.* 1955, **10**, 230.
7. Hawkins, D. F., Schild, H. O. *Ibid*, 1951, **6**, 682.
8. Pellerat, J., Murat, M. *C.R. Soc. Biol. Paris*, 1946, **140**, 297.
9. Arunlakshana, O. *J. Physiol.* 1953, **119**, 47P.
10. Goodman, L. S., Gilman, A. Pharmacological Basis of Therapeutics. New York, 1955; p. 654.

# Special Articles

## DOING WITHOUT HEROIN

DIACETYLMORPHINE, or heroin, which has been used medically for about fifty years, is recognised as the most dangerous of all drugs of addiction, and as long ago as 1931 an international conference recommended that all countries should abolish or restrict its manufacture. A number of countries, including the United States of America, took this step before the second world war; since 1949 many others have followed suit; and by 1954, in response to an inquiry by the World Health Organisation, fifty-four had expressed the view that the medical use of heroin could be dispensed with.

In this country prohibition of the manufacture of heroin has been seriously considered for more than five years. Thus on Jan. 15, 1949, the *British Medical Journal* wrote:

"The dangers of heroin are well known. Addiction is acquired more rapidly than with any other drug; once acquired, the disorder progresses with greater speed and is marked by a more profound and disastrous moral degeneration than in any other addiction. Cure is more difficult, and sudden withdrawal may prove fatal. In the light of these facts it is clearly the duty of the medical profession to examine again the therapeutic value of this substance and to weigh it against its social danger.

"Pharmacological opinion has long held that its social dangers overshadow its therapeutic importance. It must be granted that there is justice in the Permanent Central Opium Board's claim of 'an *a priori* case for its total abolition.'"

When, in 1949, the Standing Medical Advisory Committee of the Central Health Services Council was first consulted about an inquiry from the United Nations as to why the use of the drug was still regarded as indispensable, they stated that "it was favoured by many surgeons as the best postoperative sedative." On the same occasion, however, the same committee also said that, though half of the drug used in this country went into the dispensing of cough linctuses, the general opinion among physicians was that "heroin had no significant advantage over codeine or morphine as a cough suppressor." In October, 1950, the Standing Medical Advisory Committee reconsidered the alleged indispensability of heroin and decided to consult the British Pharmacopœia Commission. Later in the same year, the committee concurred in the commission's view—reached after consulting a large number of bodies including the Medical Research Council and the British Medical Association, who approved—that the advantages claimed for heroin did not outweigh the grave consequences of widespread addiction in certain countries; and the committee decided not to oppose prohibition of the manufacture and sale of heroin if international agreement on it could be reached.

In 1952 the British Pharmacopœia Commission decided to omit the monograph of heroin from the 1953 *British Pharmacopœia*.

When in 1953 the Sixth World Health Assembly recommended member States to prohibit the import and manufacture of heroin, there was a measure of support [1] and very little opposition in the British medical press. Last December the Standing Medical Advisory Committee of the Central Health Services Council was asked to consider a resolution to the same effect from the Economic and Social Council of the United Nations, and after considering the evidence which had appeared since their previous decision they agreed that prohibition of heroin was acceptable. This action was subsequently endorsed by the Central Health Services Council, which is the statutory body set up under the National Health Service Act, 1946, to advise the Minister of Health on matters relating to services provided under the Act. The results of these consultations were available to the Home Secretary and no doubt largely determined the Government's decision announced last February.

1. *Brit. med. J.* 1953, ii, 196.

### USE OF HEROIN

Last year English manufacturers made about 80 kg. of heroin for disposal in this country. Probably about half of this was dispensed on National Health Service E.C.10 prescriptions, mainly in the form of linctus of diamorphine *B.P.C.*, the remainder being used either in hospitals or for private prescriptions and proprietary preparations. It is therefore evident that quite a substantial amount of heroin is still being prescribed in Great Britain. On the other hand, in current British textbooks of general medicine and therapeutics there are relatively few references to its special value. The following, for example, is the passage on heroin in a much-used work on therapeutics.[2]

"The drug resembles morphine in its general effects, but acts more strongly on the respiratory centre. It is, therefore, more dangerous than morphine. It is more depressant to the cerebral cortex than codeine, but less so than morphine. Its analgesic effect is about 4 times stronger than that of morphine. It is excreted unchanged in the urine. Only a small degree of tolerance is acquired, and then most of the drug is destroyed in the body. No tolerance is developed towards its excitant action on the nervous system, so that convulsions may be produced in place of sleep. Addiction is common, the drug being taken in the form of snuff or by injection.

"This drug is used to allay cough, especially incessant cough with much expectoration. It is also used to abolish pain as it is less liable than morphine to cause vomiting. Alarming symptoms of respiratory paralysis may, however, occur after therapeutic doses. Papaveretum (Omnopon) is much safer and usually equally efficacious."

One [3] of the general medical textbooks contains no mention of the use of heroin, though morphine and codeine are advised; and an equally popular manual [4] of applied pharmacology, after a brief reference to its use in the treatment of cough and in postoperative discomfort, states unequivocally that "heroin is such a dangerous drug that its use has been banned in America and it would be a great advantage if this control was exercised in all other countries."

### ALTERNATIVES

Medical opinion in the United States of America, as reflected in current American textbooks, regards heroin as completely replaceable in medical treatment. Thus in one [5] work on therapeutics, of American authorship, there is the clear statement that "heroin has no indispensable advantages over morphine," and in an equally well-known American textbook [6] of pharmacology is expressed the opinion that heroin "shares all the disadvantages of morphine without any serious advantages."

That doing without heroin is a matter of the skilful employment of the available alternatives is suggested by the fact that, while some hospitals use considerable amounts, others use almost none. In his study of *Good General Practice* [7] Stephen Taylor lists the drugs carried in the bags of general practitioners: these included morphine, pethidine, compound tablets of codeine, papaveretum, and methadone, but heroin was not found in any of the bags examined.

Though there is no single drug with analgesic and cough-suppressant actions which can automatically

2. Hale Whites' Materia Medica, Pharmacology and Therapeutics. Edited by A. H. Douthwaite. 29th ed., London, 1952; p. 211.
3. Textbook of Medicine. Edited by Sir John Conybeare and W. N. Mann. 11th ed., Edinburgh, 1954.
4. Clark's Applied Pharmacology. Revised by Andrew Wilson and H. O. Child. 8th ed., London, 1952; p. 267.
5. Pharmacological Basis of Therapeutics. By Louis S. Goodman and Alfred Gilman. 2nd ed., New York, 1955; p. 238.
6. Manual of Pharmacology. By T. Sollmann. 6th ed., Philadelphia, 1944; p. 288.
7. Taylor, S. Good General Practice. London, 1954; p. 586.

replace heroin, the use of a number of other drugs, either in sequence or in combination, is held to afford equal benefits. In a recent discussion at the Royal Society of Medicine,[8] on the treatment of inoperable cancer, heroin was not mentioned, the control of pain by drugs in the terminal stages being secured by mist. acid. acetylsal. opiat., pethidine, methadone, and phenadoxone, with chlorpromazine where necessary. The intolerance of some patients to morphine, expressed by a tendency to vomit, is often put forward as a sufficient reason for the indispensability of heroin; but the coincident use of small doses of atropine and hyoscine, or of one of the antihistaminics, is said to overcome this difficulty. Another suggestion in this connection is the use of morphine combined [9] with amiphenazole (diaminophenylthiazole, 'Daptazole'). It is claimed that in this combination morphine becomes much less dangerous, and can be given in larger doses without resultant respiratory depression and without diminution of its analgesic effect.

For the control of cough there are various alternatives to linctus of diamorphine. A well-known book on general practice [10] describes linctus codeinæ as the most generally useful antitussive agent and does not mention heroin. This book also recommends linct. scill. opiat. *B.P.C.* (Gee's linctus), methadone (linctus 'Physeptone'), and for very severe cough dihydrocodeinone ('Dicodid'). The control of the severe usually unproductive cough associated with tumours of the lungs and bronchi is a difficult therapeutic problem,[11 12] for which hitherto, at least in this country, opiates including heroin have often been used. But American physicians have used alternatives for this purpose. Increasing interest is being shown in the antitussive properties of some of the new synthetic narcotics, especially in levorphan congeners such as dextrorphan and dextromethorphan. These substances, though they have no analgesic properties and are said not to produce addiction, have been found [13 14] to be as effective as codeine and to cause no undesirable side-effects.

## VITAMINS A AND D

THE nutrition panel of the food group of the Society of Chemical Industry held on Oct. 26 the opening meeting of a series concerned with Nutritional Requirements and Food Fortification. The subject of Vitamins A and D was dealt with under three headings—nutritional requirements, dietary supplies, and food fortification.

Mr. T. MOORE, D.SC., discussed nutritional requirements. He concluded that the figures of the B.M.A. nutrition committee (1949) were the most acceptable. These were based on observations in Sheffield, where 16 volunteers had been fed a vitamin-A-deficient diet for two years. Only 3 of these showed a true deficiency, which indicated that there were large liver reserves. It was shown that 1300 I.U. of vitamin A or 2500 I.U. of carotene was curative. Carotene was equivalent to vitamin A in the rat but not in man. From these figures, and including a safety margin, it was suggested that, if fed as preformed vitamin A, 2500 I.U. was adequate, or, if as carotene, 7500 I.U.; and since a mixed diet was usually composed of one-third as vitamin A and two-thirds as carotene, a total of 5000 I.U. was recommended This compared with the League of Nations (1938) figure of 2000–4000 I.U. and the United States (1943) figure of 5000 I.U. Requirements were increased in pregnancy and lactation.

The evidence for the requirements of vitamin D was very doubtful; moreover these requirements were modified by the amount of sunlight reaching the skin and the amount of calcium and phytic acid in the diet. Dr. Moore concluded that here again the B.M.A. figures were the most acceptable: children 0–2 years 800 I.U., and 2–4 years 400 I.U.; adult requirements not ascertained.

Mr. V. H. BOOTH, PH.D., dealt with the dietary supplies. The levels of intake of these two vitamins had remained very constant in recent years, even during rationing. With regard to vitamin A the absorption of carotene differed considerably according to its source. Thus carotene from vegetables was not so well absorbed as that from an oil solution, while the carotene from carrots was less well absorbed than that from green leafy vegetables. Evidence compiled by the National Food Survey showed that the average intake, corrected to vitamin A, was 3800 I.U., thus more than fulfilling the postulated requirement of 2500 I.U. Dr. Booth pointed out that this was an average figure, and that it had been shown that the coefficient of variation was 45%. It appeared that at least 16% of the population, if the distribution grouping was normal, were receiving less than 2100 I.U.

In the case of vitamin D no allowance could be made for the synthesis taking place in the skin under the influence of sunlight. From the average food intake he calculated that the intake, allowing for 15% loss, was 143 I.U. per day.

Mr. P. N. WILLIAMS discussed food fortification. Margarine was the most important vehicle for fortification with vitamins A and D and was, moreover, the first food to be fortified. When forty years ago the fat-soluble factors were shown to be present in butter it became clear that margarine was deficient in these factors; it was fortified with vitamins A and D to raise its nutritional value to that of butter. Mr. Williams traced the history of this process, which in the early days used cod-liver oil, and then later a vitamin concentrate prepared by saponifying the oil. When the potency of whale-liver oil was discovered this was used as the main source until 1939. Since there was no vitamin D in whale-liver oil this was added as irradiated ergosterol. The final stage was the use of synthetic vitamins A and D.

The vitamin content of margarine was about equal to that of butter. Other vehicles for fortification included dried milk for infant feeding, which contained added vitamin D; and in the United States tinned evaporated milk was similarly fortified.

In the discussion Miss D. F. HOLLINGSWORTH drew attention to reports of hypercalcæmia in infants said to be due to overdosage of vitamin D from the addition of enriched foods and cod-liver oil to an already adequate diet.

Mr. A. L. BACHARACH pointed out that if some children were receiving excessive doses of vitamin D and it became necessary to prevent this by reducing the amount of the vitamin in various preparations, the effect might be to exaggerate the problem of those infants not now receiving sufficient vitamin D. He suggested that this was a problem for the administrator and legislator rather than the scientist.

With reference to calciferol poisoning Mr. Bacharach expressed scepticism about the frequency with which genuine cases had occurred. Earlier reports had almost certainly referred not to calciferol but to irradiated ergosterol which contained toxic substances.

Prof. JOHN YUDKIN, the chairman, asked whether fortification of margarine raised a diet inadequate in vitamins A and D to the level of adequacy. Mr. WILLIAMS replied that margarine was likely to be the main source of vitamins A and D for people of limited income, and without this source he thought that the intake of vitamin A might be inadequate.

8. *Proc. R. Soc. Med.* 1955, **48**, 703.
9. Shaw, F. H., Shulman, A. *Brit. med. J.* 1955, i, 1367.
10. Introduction to General Practice. By D. Craddock. London, 1953; p. 516.
11. Text Book of Medical Treatment. By D. M. Dunlop and others. 2nd ed. revised, Edinburgh, 1943; p. 869.
12. Introduction to Diseases of the Chest. By J. Maxwell. 3rd ed., London, 1948; p. 146.
13. Cass, L. J., Frederick, W. S., Andosca, J. B. *Amer. J. med. Sci.* 1954, **227**, 291.
14. Ralph, N. *Ibid*, p. 297.

Professor YUDKIN drew attention to the apparent illogicality of fortifying margarine with vitamin D to a level three times as high as that of butter although the level of vitamin A was the same as in butter, particularly because infants who required vitamin D did not normally eat margarine. Mr. WILLIAMS commented that this was apparently done to provide a source of vitamin D for growing children.

In reply to a question, Miss HOLLINGSWORTH pointed out that there was little difference between the nutritional intakes of different income-groups, in contradistinction to the state of affairs in the 1930s, and that the greatest differences were between families with different numbers of dependants.

## PLANNED PARENTHOOD

### International Conference in Tokyo

FROM A CORRESPONDENT

THE theme of the 5th International Conference on Planned Parenthood, held in Tokyo from Oct. 24 to 29, was overpopulation and family planning. A vast array of material was presented—the Japanese alone offered more than 30 papers—covering demographic and clinical studies, field trials, and fundamental research aimed at the control of fertility.

In an arresting paper Dr. Elmer Pendell argued that the concept of "the dignity of the individual" could be carried so far as to clash with the interests of society. Not only must quantity of population be controlled; quality also must be maintained by a judicious policy of sterilisation. Dr. Frederick Osborn held that society should make easier early marriage and large families for its more valuable stocks—i.e., those conspicuous for vitality and early achievement.

Defining population pressure as "the way a people feels about its own economic situation as compared with that of other peoples," Prof. Warren S. Thompson gave reasons for expecting this to increase in the next few decades. In his view population pressure was one important cause of, but did not lead inevitably to, war.

Though the dangers of overpopulation are appreciated the world over, it is significant that so far the governments of only two countries—India and Japan—are realistically facing them to the point of financing family planning programmes. That Communist China is alive to this danger is shown by the fact that a request was received at the last minute from the Peking government for permission to send delegates to the Tokyo conference. Unfortunately, though the request was readily granted, it was too late for the Chinese to make the necessary arrangements.

Reports were made to the conference of a number of field studies, notably the Ludhiana experiment and the successful experiment, under the direction of Prof. Yoshio Koya, at present under way in three villages in Japan.

The most important feature of the conference was the fact that many distinguished scientists were gathered together to describe their researches into reproductive physiology and to exchange ideas. Though the perfect agent for the control of fertility is not yet in sight, various promising lines of investigation are being pursued. Attempts are being made to select stages in the male and female reproductive processes which are vulnerable to designed interference. Among the oral contraceptives being examined are certain antimetabolites, progesterone-like substances, anti-histamine agents such as ergotoxin, and the recently isolated active principle of *Pisum sativum*, metaxylohydroquinone.

### Family Planning Association

As part of its 25th-anniversary celebrations the Family Planning Association held its second conference of doctors and nurses on Nov. 26.

#### SUBFERTILITY

Dr. G. I. M. SWYER described a routine preliminary approach to subfertility cases which could be applied in any clinic without special facilities, and would deal with most of the simpler problems. But he stressed the importance of post-coital testing and semen examination by experienced staff.

#### MARITAL PROBLEMS

Dr. A. G. THOMPSON opened a discussion on the provision of advice on marital difficulties. The general feeling was that a large proportion of the difficulties which patients mentioned, though a source of real unhappiness, could be very simply dealt with by a few understanding words and a background of common sense. It was important to give patients an opportunity to voice their worries. Many felt that they were abnormal and were anxious about the abnormality. To be told that their problem was common and easily resolved was often all the help they needed. Doctors who were also marriage-guidance counsellors felt that the more difficult problems were best referred to marriage-guidance centres. But clinic doctors were in a unique position for helping people with simple and common problems. The majority of F.P.A. clinics appeared to provide such a service, and many worked in close coöperation with the Marriage Guidance Council.

#### UNPLANNED PREGNANCIES

Dr. MARGARET HADLEY JACKSON described an investigation into the causes of unplanned pregnancies in clinic patients. From the figures given by Dr. Jackson and other speakers it appeared that a surprisingly large number of patients gave up using the occlusive-cap and paste method of contraception because they found it unacceptable.

#### BIRTH-CONTROL

Dr. NAOMI PENFOLD spoke about how the unconscious motivation of patients might affect their acceptance of a birth-control method. Many patients were ambivalent about further pregnancies; some were unenthusiastic because it would mean resumption of intercourse with the spouse. A subfertile woman had enormous motivation to become pregnant; most women had a far less intense desire not to become pregnant. Many women felt that birth-control was the husband's responsibility; but it seemed best that where psychological disorder was present the responsibility should be with the more stable partner.

---

Mr. IAIN MACLEOD, the Minister of Health, during a visit to the North Kensington centre of the Family Planning Association on Nov. 29, said that the position held by the association today would have seemed unthinkable to the pioneers of the movement twenty-five years ago. Happily, he said, much of the prejudice and ignorance about its work had been swept away, and today many local authorities sent patients to the association's centres rather than start their own clinics. Mr. Macleod referred to the admirable work done in planning the size of families; helping women who, for medical reasons, had been advised to have no more children; and teaching doctors, nurses, and senior students contraceptive technique. In congratulating the association on bringing happiness and fulfilment to many families, Mr. Macleod added that there were thousands of people in this country whose different views on family planning we should respect.

The Family Planning Association was started in 1930, to coördinate the work of five existing organisations. Lady Denman, who helped to found the association, was chairman until she died last year. Lord Horder was the first president, and still held office at the time of his death. The association maintains an approved list of proprietary contraceptives; and at its headquarters, 64, Sloane Street, London, S.W.1, there is a pregnancy diagnosis laboratory where the results of Hogben tests are available in twenty-four hours. Last year the association's 198 centres in England, Scotland, and Wales were visited by about 200,000 patients, mostly for the first time. Fees are charged according to the patient's means. The North Kensington centre, which was opened in 1924, deals with all aspects of family planning, including helping childless couples to start a family. (The association estimates that as many as 10% of all married couples may be involuntarily childless). Some 20,000 patients have already been seen at the London medical centre for the investigation of male infertility, which is the first of its kind in the country.

# GENERAL MEDICAL COUNCIL

SESSION NOV. 22–25

BEFORE Sir DAVID CAMPBELL'S presidential address[1] at the 191st session of the General Medical Council on Nov. 22, two new members were introduced and took their seats—Mr. HEDLEY ATKINS, representative of the Royal College of Surgeons of England, and Mr. VICTOR LACK, representative of the Royal College of Obstetricians and Gynæcologists.

Dr. H. GUY DAIN presented the report of the Pharmacopœia Committee, incorporating the report of the British Pharmacopœia Commission, 1953–58. Sales of the *Addendum, 1955*, had been extraordinarily good—much better than those of the previous *Addendum*. Work on the next *Pharmacopœia* was well in hand. Among the matters which the Commission had considered was the colouring of tablets. After careful consideration, they recommended that the requirements stated in the *Pharmacopœia* should be retained. The Pharmaceutical Society and the representatives of retail pharmacists strongly supported the retention of the present ruling.

The council considered the report of the Committee for the Registration of Commonwealth and Foreign Practitioners. They agreed that for the purpose of section 1 (*b*) of the Medical Act, 1950, the following should be regarded as having had the compulsory houseman experience specified in section 4:

Persons holding recognised diplomas granted after Jan. 1, 1953, by the University of Malaya who are registered as medical practitioners in the colony of Singapore or the Federation of Malaya.

Persons holding recognised diplomas granted by the University of Sydney who produce a certificate of hospital service given by the New South Wales Medical Board, provided that the person's experience, as shown on the certificate, satisfies the requirements of the Act.

Persons holding recognised diplomas granted by the University of Dalhousie after Jan. 1, 1929, who are registered as medical practitioners in Nova Scotia.

Persons holding recognised diplomas granted by the University of Manitoba after Oct. 20, 1948, who are registered as medical practitioners in Manitoba.

## Medical Disciplinary Committee

The committee began its session on Nov. 23, with the President in the chair. During the President's absence on Nov. 24, Prof. R. J. BROCKLEHURST took the chair.

### APPLICATIONS FOR RESTORATION

*Sumatapalage Reginald Gunewardene* applied for restoration of his name. He had been told that he could not be put on the Register in Ceylon while his name remained off the British Register. The committee did not see fit to direct the registrar to restore the applicant's name.

*Archibald Luke Basham*, whose name was erased in August, 1954, following his conviction for conspiracy to defraud an executive council, applied unsuccessfully for restoration.

*Robert Vivian Storer* applied for restoration of his name, which had been erased in 1935. His name was not restored.

The registrar was directed to restore the name of *Arthur James Daly*.

### INTENT TO PROCURE MISCARRIAGE

*Basil Arthur Furniss*, registered as of 1, Dean Park Road, Bournemouth, Hants, M.R.C.S. (1939), was convicted in July on three charges of unlawfully using an instrument with intent to procure the miscarriage of a patient. The committee directed the registrar to erase his name from the Register. This decision is subject to appeal within 28 days.

### NOT ERASED

In November, 1953, the committee postponed judgment in the case of *William Francis Hirsch Coulthard*, registered as of Balwinnam, Aspatria, Carlisle, M.B. Edin. (1927), in order to give him a further opportunity of overcoming his tendency to drink to excess. In view of the satisfactory information they had received concerning Dr. Coulthard's conduct, the committee decided not to direct the registrar to erase his name.

Judgment had also been postponed in the case of *William Bellamy James*, registered as of 41, University Road, Belfast, M.B. Belf. (1938), who was convicted in 1951 and 1954 of driving a motor-car while under the influence of drink. The committee did not direct the erasure of his name.

*Boris Nicholas Klukvin*, registered as of 6, Normanton Terrace, Newcastle upon Tyne, had been convicted of motoring offences concerning drink and dangerous driving in 1940, 1951, and 1954. Judgment had been postponed for one year in November, 1954. The committee decided not to direct the registrar to erase his name.

*John Lennon*, registered as of Springfield, Castleford, Yorks, L.M.R.C.P.I. (1929), had been convicted of disorderly conduct whilst drunk (in 1930) and of drunkenness in charge of motor vehicles (in 1935 and 1954). Judgment had been postponed in November last, and the committee now decided that Dr. Lennon's name should not be erased.

*Alexander Urquhart*, registered as of 8, Portland Street, Troon, Ayrshire, M.B. Glasg. (1947), had been convicted in 1950 of driving a motor vehicle when under the influence of drink or drugs and in 1954 of being in charge of a motor vehicle when under the influence of drink. Judgment had been postponed for one year. In view of the satisfactory information received as to his conduct, the registrar was not directed to erase his name.

The committee had previously postponed judgment for one year on *Patrick Laurence Lyons*, registered as c/o District Bank Ltd., 55, King Street, Manchester, L.A.H. Dubl. (1948), who had been fined for being drunk and disorderly. The committee did not direct that his name should be erased.

### JUDGMENT POSTPONED

*George Ralph Spencer Jackson*, registered as of 1, Penistone Road, Sheffield, 6, L.M.S.S.A. (1943), had been convicted of being in charge of a motor-car when under the influence of drink. Judgment was postponed until November, 1956.

In the case of *Joseph Hirschemann*, registered as of Upper House, Clunbury, Craven Arms, Salop, M.B. Dubl. (1920), judgment had been postponed following convictions under the Dangerous Drugs Act. After consideration in camera, judgment was again postponed for a further 6 months.

*Joseph White O'Brien*, registered as of 176, Sewardstone Road, Victoria Park, London, E.2, M.B. N.U.I. (1914), appeared because of a series of convictions; the last was for driving a motor-car when under the influence of drink in March this year. It was stated that Dr. O'Brien had been under treatment in hospital since March. Judgment was postponed for two years.

### NO POLICE INFORMATION

*Alexander Winchester St. Clair Greig*, registered as of 26, Kersland Street, Glasgow, W.2, M.B. Glasg. (1935), had been convicted on three occasions of driving when under the influence of drink. Mr. G. J. K. Widgery, solicitor to the General Medical Council, said that, as happened in Scottish cases, he had been unable to obtain any details from the police in Glasgow. Dr. Greig was not represented, but Mr. Widgery read a letter from an Edinburgh solicitor which stated that, following the last conviction, sentence had been deferred for the doctor to obtain treatment in a mental hospital. Dr. Greig said that at the time of the last offence he had had a slight blackout and could not remember what had happened. He was now under treatment. The committee postponed judgment for two years.

### DRUGS FOR WIFE

*Peter Louis Milbourne Hartley*, registered as of 408, Wimbledon Park Road, London, S.W.19, M.R.C.S. (1941), M.B. Camb. (1946), had had judgment postponed for one year following convictions of unlawfully procuring drugs. The drugs were for his wife. He had not been treating her at all since the conviction. She had been discharged from hospital "apparently cured" in April. The committee did not direct the registrar to erase Dr. Hartley's name.

### INFAMOUS CONDUCT

In November, 1953, the committee postponed judgment for two years in the case of *William Arthur McIlrath*, registered as of 222, Lewisham Way, London, S.E.4, M.B. Belf. (1928). The charges related to being on the medical list of the London Executive Council and receiving grants for the training of a trainee assistant, when Dr. McIlrath was employed in a whole-time capacity at a hospital. The committee found Dr. McIlrath guilty of infamous conduct in a professional respect, but after considering the satisfactory information as to his conduct, they did not directed the registrar to erase his name.

### IMPROPER CERTIFICATES

*Harvey Forrester Jackson*, registered as of Johnene, Leighinmohr Avenue, Ballymena, co. Antrim, M.B. Belf. (1949), appeared for judgment postponed from November last year, when the committee found that he had issued documents over his signature which were, in the circumstances, misleading and

1. See *Lancet*, Nov. 26, 1955, p. 1132.

improper, to assist persons to obtain houses of the Belfast Corporation. The committee found him guilty of infamous conduct but in view of the satisfactory information as to his conduct, they did not direct the registrar to erase his name.

### CONSPIRACY TO DEFRAUD

*Adam Clark*, registered as of 1, Harley Street, London, W.1, L.M.S.S.A. (1929), had been convicted of conspiring with other persons to cheat and defraud by administering drugs to greyhounds.

Mr. Widgery said that Dr. Clark was in practice in Bournemouth and had an address in Harley Street. He became friendly with a man named Green, who some months later introduced him to another person named Selby. They met and discussed the effect of drugs on greyhounds. Dr. Clark admitted supplying drugs to Green and that some of the drugs were for use by medical practitioners only. For Dr. Clark, it was said that the drugs were never used on dogs in general, and Selby had said that he injected only a small amount of hydrocortisone into one sick poodle who never ran in any race. A long statement had been taken from Dr. Clark by the police without warning. It was clearly a statement obtained from Dr. Clark in order that he could give evidence for the prosecution: in fact, it was used against him.

The chairman announced that the committee took a grave view of the conviction. They were, however, prepared to take into consideration the representations made on Dr. Clark's behalf and the evidence concerning his character. They had decided to postpone judgment for two years.

### A TREATMENT FOR BALDNESS

*John Kelvin*, registered as of 1446, Dumbarton Road, Glasgow, W.4, L.R.C.P.E. (1925), M.B. Leeds (1926), appeared on a charge of infamous conduct in a professional respect. It was alleged that, for his own professional advantage, Dr. Kelvin associated with an organisation known as the Akers Hair and Scalp Clinics in the United States, which had systematically procured or sanctioned the publication in various American newspapers of reports and advertisements directing attention to his professional skill, knowledge, services, and qualifications; and that in furtherance of the association he held a press conference in Chicago in October, 1954, all contrary to section 6 (c) of the Warning Notice.

Mr. Widgery stated that Dr. Kelvin was in practice in Glasgow. In September, 1954, a letter from Dr. Kelvin appeared in the *British Medical Journal* under the heading Cure for Baldness. This described how two of his patients to whom he had given β-pyridyl-carbinol tablets ('Ronicol') for intermittent claudication "proudly and happily volunteered the information that the tablets had grown a good crop of hair on their bald pates." That was a perfectly proper letter for a medical practitioner to write to a professional journal, Mr. Widgery continued. But it was taken up in the popular press and Dr. Kelvin seemed to have been involved in a blaze of world-wide publicity. He said in a letter to the registrar: "I was written up in every newspaper and every magazine in every town in every country in the world. My telephone buzzed incessantly. News reporters and correspondents harassed me unmercifully."

The director of the Akers Hair and Scalp Clinics came to Glasgow and was photographed with Dr. Kelvin at Prestwick airport. He offered to open a research laboratory in Glasgow with Dr. Kelvin as research director at a salary of $10,000 a year. Mr. Widgery said that Dr. Kelvin was obviously dazzled by the commercial prospect before him, and provisional terms were agreed. On Oct. 24, 1954, Dr. Kelvin flew to America to sign the contract. He wrote a letter to the General Medical Council asking for his name to be removed from the Register. In Chicago a press conference was held, where Dr. Kelvin was photographed examining the bald head of a patient. There were further negotiations, but he was put off and no contract appeared. Dr. Kelvin came back, no doubt disillusioned, to Glasgow. He found a letter from the registrar explaining that formalities had to be complied with before his name could be removed from the Register.

Further negotiations went on. The Akers Clinics put numerous advertisements in American newspapers long after Dr. Kelvin returned to Scotland. One advertisement included a letter supposedly written by Dr. Kelvin and signed by him. The doctor denied authorship of the letter, and the signature, so far as Mr. Widgery had been able to ascertain, did not appear to be his.

Mr. James Colquhoun, a solicitor, said that he was a partner in the firm of Graham and Co., of Glasgow, and that the Akers Hair and Scalp Clinics were clients. His clients offered Dr. Kelvin an appointment as research director; he would have conducted his research in Glasgow. Mr. Colquhoun agreed that the Akers organisation wanted to get hold of Dr. Kelvin and use his name. "Did you persuade him to give up his practice in Glasgow?"—"No. It was pointed out to him that he would probably have to." Mr. Colquhoun was asked whether any photographs were taken at the press conference in Chicago. He replied: "Oh, yes. These Americans go in for it in a big way. We had Kleig lights and everything. A reporter said: 'Look at my head, doctor.' Dr. Kelvin looked and he was taken." He did not remember Dr. Kelvin signing the letter. Heads of agreement were signed before Dr. Kelvin went to America. The object of the visit to America was to sign the final contract, but no such agreement ever came into being.

Cross-examined, Mr. Colquhoun agreed that Dr. Kelvin was at all times anxious to safeguard his professional position and that he was anxious not to do anything while he remained a doctor which conflicted with his duties. He wanted to safeguard his position as a doctor until he actually joined the Akers organisation. Mr. Colquhoun said that Dr. Kelvin was looked on as research director in the Akers organisation and received sporadic payments—about four—of $500 a month.

In evidence Dr. Kelvin said that when he went to America he did not know that he was to be the subject of publicity. When he went to America he had a shock when he found he was among crooks and profiteers. The contract was never signed. He was to be paid full expenses for his trip to America but when he got there the Akers organisation refused to pay his hotel expenses. When he returned to Glasgow he received four sporadic payments of $500. Asked about the letter, he said it was a complete forgery from beginning to end; he did not write it and he did not sign it.

Cross-examined, Dr. Kelvin said that he was to have had $500 a month in addition to the profits and properties of two clinics. He lost more than he got from Mr. Akers. Of the press conference in America he said: "I was press-ganged into it. I was dazed and confused by the whole proceedings." He did not know whether it was being broadcast or televised. When he went to America he was under the impression that he was off the Register.

After deliberating in camera, the committee concluded that the facts alleged against Dr. Kelvin were proved to their satisfaction, and they regarded the charge with grave concern. They decided to postpone judgment for two years.

### A CONVICTION IN MALAYA

*Bak Hin Ong*, registered as of 10, Riverside, Malacca, L.R.C.P.E. (1915), had been convicted in 1953 in the High Court of Malaya of having unlawfully performed an operation of abortion which caused the death of Tee Bee Geok.

Mr. Widgery explained that under section 29 of the Medical Act of 1858 this case, being a conviction outside the United Kingdom or Eire, had to be treated as one of conduct. He therefore had to prove to the satisfaction of the committee the charge against the doctor. He proposed to rely for his evidence on the transcript of the trial in Malacca. Later in the proceedings it was stated that this was the judge's note, not a shorthand transcript.

Mr. N. L. Taylor, appearing in his private capacity for Dr. Ong, objected to the evidence being received in this form on so serious a charge. Dr. Ong had come 8500 miles to be present. Whatever might have been done in Malacca, he felt that here he would get an absolutely fair trial. The committee could not give a fair trial without the witnesses. Mr. Widgery had not suggested that the witnesses could not be produced. It might be inconvenient and an expense: Dr. Ong had been put to inconvenience and expense.

The legal assessor, Mr. C. P. Harvey, Q.C., said that the council could not compel the attendance of witnesses. They were back to the position of the General Medical Council before the Act of 1950. On the basis of the decision in the Spackman case, he felt bound to advise the committee that this method of admitting evidence remained open to them and indeed must be employed. A civil court, in litigation, could direct a commission to go out to Malacca to take evidence, and a criminal court would simply decline jurisdiction; but the committee could do neither of those things.

In consultation with Mr. Widgery, but not with Mr. Taylor, Mr. Harvey had been very carefully through the transcript, since under the rules he had to advise the committee what statements contained in documents ought to be received.

The transcript contained many passages which would not be received in this country, and in the copies of the transcript for members of the committee, these had been excised. The legal assessor also advised the committee not to read the judge's summing-up.

Mr. Widgery then stated his case, with reference to the transcript. He alleged that the Chinese woman, Tee Bee Geok, came to see Dr. Ong at his maternity home without the knowledge of her husband. She told the doctor that she had 7 children and did not want to have more. The doctor agreed to help her and an immediate operation was performed. She went home by bus and pedicab. Next day the husband found his wife seriously ill. He took her to hospital, where she was found to have a perforated uterus. She died two days later.

Mr. Taylor said that Dr. Ong's family had lived in Malacca for 300 years. He was a rich man who did not have to rely on medicine for his living. The esteem in which he was held was not restricted to the Chinese community. He occupied public positions and was a member of the Chinese consultative committee set up to advise the government. There was antipathy between indigenous Chinese and immigrant Chinese. What could be more readily at hand to discredit a political opponent, asked Mr. Taylor, than this charge? The dead woman's husband, he alleged, was a member of a certain political party.

Turning to the evidence, Mr. Taylor said that Tee Bee Geok came to Dr. Ong saying that she did not want to have more children. She had been taking drugs. Dr. Ong concluded that she had had a partial miscarriage, and being used to dealing with emergencies among women who would not go to hospital, he evacuated the uterus. In evidence, Dr. Ong said he had never in his life performed an abortion without having therapeutic grounds for doing so. He examined the clots which came out of the uterus and did not see an ovum. He did not agree that his instrument had caused the perforation.

After deliberation in camera, the committee found the facts alleged proved to their satisfaction, and the registrar was directed to erase Dr. Ong's name from the Register.

## MUSEUM OF COLLEGE OF SURGEONS

Sir Henry Dale, O.M., F.R.S., opening the Wellcome Museums at the Royal College of Surgeons of England on Nov. 23, recalled that the Hunterian Museum and much of its precious contents suffered grievous damage during the air attacks of 1941. The rebuilding and extension of the college had been planned, he said, over ten years ago, but lack of funds prevented the construction of new museums until the Wellcome Trustees gave £100,000 for this purpose. The late Sir Henry Wellcome, the founder of the Trust, was an honorary fellow of the college.

The museums occupy three floors immediately above the new Great Hall, and form integral parts of the departments of anatomy and pathology. The lower floor consists of a pathological exhibition room, the offices of the curator (Dr. L. W. Proger), a research laboratory, a preparation room, and a workshop. The exhibition room is spacious and is divided into five bays; it has a wide central aisle which can be used for temporary exhibitions. "Natural" fluorescent lighting and neutral-grey walls behind the shelves display the specimens to advantage. The layout of the museum on the floor above is similar and houses the Hunterian Collection as well as selections from the odontological and war collections. There is also a photographic unit on this floor. The upper floor comprises the museum of anatomy with the offices of the conservator (Prof. G. W. Causey), a workshop and mounting-room, an embalming and preparation room, and the prosectors' room. The anatomical specimens will eventually be arranged according to the various systems of the body, illustrated by tracings and diagrams of physiological and pharmacological reactions where appropriate; but until the rest of the building is completed the museums will continue to house the Hunterian physiological and anatomical collection, and demonstration classes. Laboratories of the Imperial Cancer Research Fund are also being temporarily accommodated in the museums.

# In the Mental Hospital *

## INSTITUTIONALISATION

DENIS V. MARTIN
M.R.C.S., D.P.M.
CONSULTANT PSYCHIATRIST AND DEPUTY PHYSICIAN-SUPERINTENDENT, CLAYBURY HOSPITAL, WOODFORD BRIDGE, ESSEX

THE words "becoming institutionalised" or "well institutionalised" are often to be found in the clinical notes of mental hospitals. These phrases cover two stages in a process which has come to be accepted as the most desirable one for the chronic patients in our mental hospitals.

"Well institutionalised" implies that the patient has ceased to rebel against, or to question the fitness of, his position in a mental hospital; he has made a more or less total surrender to the institution life. When the nurses are asked about the progress of an institutionalised patient, the usual reply is: "He gives no trouble, doctor, he is very coöperative." Here "coöperative" usually implies that the patient does as he is told with a minimum of questioning or opposition. This response on the part of the patient is very different from that true coöperation, essential to the success of any treatment, in which the patient strives to understand, and work with, the doctor in his efforts to cure.

The "well-institutionalised" patient, resigned and coöperative, who has ceased to question his position as a patient, and who has become too passive to present any problem of management, has in the process of necessity lost much of his individuality and initiative. It may be that institutionalisation is, in fact, the most desirable end for the mass of the chronically insane who are beyond the reach of treatment, and who have to be cared for under difficult conditions for the rest of their lives. But far too little attention has been paid to the effect that this process has on the treatment and prognosis of the early cases who are admitted to our mental hospitals. Little has been written on this subject, and there seems to be widespread unawareness of the power that the institution exerts on the patient when he is first admitted to hospital and is still accessible to treatment.

### The Patients

What brings a patient to this state of institutionalisation? Some would argue that such a state is the predetermined end of some forms of mental disease. Schizophrenia is the disease most likely to produce this state. Does the natural end-result of this common mental disease influence us unconsciously to produce similar results in other patients because of its trouble-free effect? Institutionalisation is not confined to one diagnostic class. In any mental hospital will be found recovered depressives who no longer need remain in hospital on account of their original illness, but who now lack any desire to leave it. The same is true of some neurotics, alcoholics, and other groups of patients. Yet it can hardly be argued that mental illness in general, regardless of its type, produces an end-state similar to "institutionalisation."

#### BEFORE ADMISSION

Factors outside the hospital, such as inadequate personality and lack of satisfying interests and relationships, may predispose a patient to become institutionalised; and unfavourable economic circumstances probably add their weight. These external facts should not divert our attention from the power of the institution to mould

* A group of articles chiefly concerned with the value of active occupation and work for mental patients and the means whereby it is best provided.

patients into the type best suited for its purpose. Indeed, it is for those who are predisposed that the danger is most acute.

Before a patient agrees to enter hospital, unless relatives have exerted undue pressure, he is usually suffering considerably. This suffering is the strongest force driving him to seek a solution to the problem of his illness. Besides this suffering, inherent in his illness, he has also had to bear some material discomfort—e.g., loss of wages and the luxuries and entertainments that money can buy. Moreover, while at home he is constantly aware of the unhappiness that his illness causes his family and which may be expressed in ways that are painful to him. Some responsibility is still thrust upon him. All these factors tend to keep alive in him the urgent necessity of solving the problem of his illness in some way.

### THE FIRST WEEK

Entry into hospital at once removes many of these anxieties; and many patients, particularly neurotics, feel much better soon after admission. This can be accounted for by their removal from the responsibilities and personal relationships that are productive of suffering, but it immediately lessens their drive to solve their difficulties. It is the first step towards institutionalisation. Entry into hospital has given relief and offered protection, but they are seldom aware of what has happened, and so do nothing to save themselves from further drift away from their problem. This lessening of symptoms on admission to hospital resembles the initial symptomatic relief often obtained in individual psychotherapy, before any awareness of the dependence in the transference relationship is established. In individual treatment the doctor is aware of this situation and takes steps to make his patient aware of it also; if he does not do so, treatment ceases to progress. In the institution, however, the patient is seldom deliberately made aware of his position in relation to the hospital, largely because the staff are themselves more or less unconscious of the way in which the institution influences the patient; in fact, they often foster this dependence by their relatively unconscious participation in the organisation of the hospital.

The power of the institution is further shown by the fact that some patients, who may for a few weeks be aware of their true position, are gradually drawn into this state of unconsciousness as the hospital exerts its influence on them; they "settle down," to use another phrase commonly found in the clinical notes of any mental hospital.

Once in hospital the patient quickly becomes absorbed into its highly organised life. The fact that any large institution needs an efficient and complex organisation carries with it the danger that the life of the individual within it will also become highly organised, and this will tend to relieve him of the need to think or plan for himself in any but the most unimportant trifles. His basic needs are supplied, his meals are prepared at the appointed time, he is given a bed to sleep in, and facilities for washing. Outside the hospital these basic needs are usually his own responsibility; his illness is a threat to their supply, and they are a powerful incentive to recovery. The patient's recreational needs are also met without any real effort or thought on his part. Cinema, television, cricket, musical evenings, and debates are organised for him either by the staff or by a few more enterprising patients. Many patients get more positive pleasure out of life through the amenities of the hospital than they obtain outside.

### OCCUPATIONAL THERAPY

The occupational régime also plays a part in institutionalisation in the average mental hospital. Some patients are put to work in the utility departments of the hospital. These departments must be run with the economic efficiency of the hospital as the first consideration, and so it is inevitable that the patients working in them become more or less involved in this necessity. As a result the productivity of the department becomes more important to the hospital than the effect that the work is having on the patient. He finds himself working in the interests of the institution instead of in his own interests, but he is seldom aware of this. Thus a patient may be lost in the routine work of a single department for many months, without anyone questioning the wisdom of this. Again, the transfer of a patient from one type of work to another for therapeutic reasons may be strongly resisted because he is, in the language of the clinical notes, such a "good worker."

Many patients are sent to work in the occupational-therapy department. Some of these departments are also in danger of becoming production houses for the hospital. The chief criterion of their worth is often the quality of the annual exhibition or the number of useful articles produced for the hospital, rather than their value to the patient as therapy. More often the occupational centre is regarded as a purely therapeutic department, but even then the aim of too much of the work is merely to alleviate symptoms. Thus anxiety is allayed by a "soothing craft," or new interests are created to take the patient's mind off his symptoms. Such an approach may relieve suffering, but it adds to the patient's dependence on the institution, and deflects him from the task of solving his inner problems.

## The Staff

Refractory wards, where violent and destructive patients and those who tend to wander away are segregated, tend to be regarded by the other patients as a place of punishment to which they will be sent if they do not conform to the accepted pattern of hospital behaviour. Thus a patient is inhibited from criticism of the staff or of the organisation of the hospital, or from using initiative, lest he be transferred to the refractory ward about which he has frightening fantasies. The danger inherent in refractory wards is that staff may solve difficult problems of behaviour by the easy way of transferring the patient to the refractory ward rather than by careful inquiry into possible faults of organisation or personal relationships which may, in fact, have been the cause of the patient's behaviour. Thus, the staff become victims of the system and are prevented from helping patients as much as they might if they examined the situation more critically. The pattern of behaviour usually expected from the patient is similar to that of the "well institutionalised." The staff are rarely aware that they, too, are influenced by the pattern of life in the institution. Unconscious, or unacknowledged, motives for transferring a patient to a refractory ward are easily rationalised under the present system.

### THE DOCTORS

The problem of the refractory ward leads naturally to an examination of the part played by the medical staff in fostering, largely unconsciously, the crippling process of institutionalisation. A number of factors render the doctor vulnerable to the powerful influence of the institution. The most obvious predisposing cause is the size of his problem. He is responsible for anything from 100 to 300 patients, and the tendency of the organisation to produce "well-institutionalised" patients simplifies his task; the patient who gives no trouble leaves more time for the treatment of those who satisfy the doctor's particular therapeutic interests. Thus he has, as it were, a vested interest in maintaining the process of institutionalisation.

Again the doctor's own personality difficulties, which lead to a sense of insecurity, predispose him to become a

victim of the institution that he is helping to run, in much the same way as such difficulties affect the patient.

The doctor's tendency, often unconscious, to hide behind his traditional professional status is also a powerful influence in the process of institutionalisation. This tradition makes it difficult for him to communicate with junior nurses except through the ward sister, and even more difficult to communicate with employees in the utility departments except through the heads of departments. Thus the people most closely in contact with the patient are often either unaware of their real therapeutic rôle, or are unable to coöperate adequately with the doctor. Too often, as a result, they succumb to routine and disillusionment, or the patient comes to be regarded as just another employee. This situation is made clear by the astonishment, or overwhelming gratitude, of a junior nurse when a doctor does, for some reason, take the trouble to discuss a patient with him as a real partner in the task of understanding and treatment, instead of regarding him as someone who merely carries out specific directions.

A doctor who pays at least lip-service to the importance in individual psychotherapy of those fantasies of the patient which lead him to view the doctor as all-powerful and all-wise, may yet be unaware of the influence that his status as a member of the medical staff of the hospital has on the patient. One patient expressed this clearly when he said, "You are my doctor, but you are also a member of the staff." He sensed that the man whom he might trust as a doctor might yet resort to punishment in the name of the institution to preserve the peace. Mental-hospital doctors are often caught in this dilemma, and they often sacrifice their relationship with the patient rather than detach themselves from the authority of the institution. They may feel such detachment to be an act of defiance or disloyalty to a senior member of the staff—e.g., the superintendent. In hospitals where rules are prominent this conflict appears insoluble, since disloyalty or defiance to an authoritarian system may create chaos; on the other hand loyalty or submission often interferes with the doctor-patient relationship.

A doctor must be well integrated and secure within himself if he is to preserve a high degree of consciousness within the organisation of a mental hospital of which he is a part. Only thus can he deliberately help his patients, avoid the evil effects of institutionalisation, and remain a responsible member of the staff.

### THE NURSES

When we turn to the influence of the nursing staff in this process we have first to consider the nurse's training which, far more than the doctor's, is destructive of individuality. The doctor has more freedom to express what is characteristically individual in his personality; he is not expected to toe the line, or obey orders, to the same degree as the nurse. Moreover, too little training in the understanding or management of human relations is given to the mental nurse, yet skill in such relations is probably his most desirable qualification. This, in itself, makes him feel insecure and inclined to fall back on a rigid system to maintain his status. To the extent that he lacks ability to form real relations with his patients, to that extent must he fall back on the authority of the institution. The obstacles to his becoming conscious of this situation are also greater than for the doctor. So long as the quietness and tidiness of the ward, based on submission to the institution, is the conscious, or unconscious, criterion of nursing efficiency, the nurse's task must remain largely that of maintaining a relationship of authority and submission between himself and the patient. Failure on his part may, in fact or in fantasy, threaten him from above with loss of promotion or favour, and this strikes at his home life where promotion means material security. He feels that it is dangerous for him to act too much as an individual towards his patients. So long as he is wholly, or partly, under the power of such a system he is likely to foster the process of institutionalisation, and to be incapable of a relationship with his patients which might help to save them from this process.

### Conclusion

I have made no attempt to do more than open up for thought and discussion what I feel to be a most important problem in the treatment of psychiatric disorders in hospital. The ideal solution would be to staff our mental hospitals only with men and women sufficiently independent and integrated to replace an authoritarian system by real human relationships. Such a staff is pure fantasy, and such a notion offers no practical answer to our problem. Since the tendencies to institutionalisation are likely for the present to remain, it is the more important that psychiatrists working in mental hospitals should increase their own awareness of the problem, and that of their nurses, and take what steps they can to help their patients to become conscious of this danger, lest they join the ranks of the "well-institutionalised."

## Medicine and the Law

### Death from Intestinal Obstruction

IN the Scottish Court of Session on Nov. 11, Lord Strachan awarded damages against a house-surgeon and a hospital board of management for professional negligence in connection with the death of a patient from intestinal obstruction.

A 47-year-old man had a minor operation on his foot on Feb. 8, 1951, while a hospital inpatient. He was quite well immediately after the operation but on the morning of Feb. 11, he had nausea and pain in the upper abdomen. The house-surgeon found nothing wrong with him and prescribed magnesium trisilicate for a "gastric upset." The patient vomited twice that day and refused food.

He vomited again at 2 A.M. next day (Feb. 12), and was seen during a routine ward-round that afternoon by the consultant surgeon, who could find nothing seriously wrong; he told the house-surgeon to keep an eye on the patient, who had a bowel motion that day for the first time since his operation.

Next day (Feb. 13) the patient vomited twice and had abdominal discomfort, but he was not seen by the house-surgeon from that morning until 7 P.M. on Feb. 14, when he vomited dark-brown, foul-smelling fluid. The patient's abdomen was distended and the house-surgeon suspected intestinal obstruction; he ordered an enema which yielded a good fæcal result but little flatus. The distension subsided, and he decided that there was no obstruction. At 10 P.M. the patient's pulse-rate, which had been steadily rising since the morning of Feb. 13, was 120 per min.

At 2 A.M. and 4 A.M. on Feb. 15, the patient vomited after drinking some water, and later he vomited some foul-smelling fluid; but at 8.45 A.M. the house-surgeon considered his condition no worse. At about 10 A.M. the patient collapsed and vomited a copious amount of intestinal contents; the consultant surgeon diagnosed intestinal obstruction, and at operation at another hospital that night a complete obstruction of the upper bowel was found, which the surgeon estimated had been present for about thirty-six hours. The patient's circulatory collapse could not be reversed and he died the next day (Feb. 16).

Lord Strachan acquitted the house-surgeon of negligence in failing to diagnose the condition, but held that had he exercised ordinary care he would have informed his seniors of the patient's condition (which he had good grounds to believe was serious) on the night of Feb. 14: had he done so, Lord Strachan said, the patient's life would probably have been saved.

Damages were apportioned equally between the house-surgeon and the hospital's board of management.

# In England Now

*A Running Commentary by Peripatetic Correspondents*

THE installation of the Queen Mother as Chancellor of the University of London was in the finest tradition of academic ceremony. The processions of the senate and higher officers, the representatives of other universities, and the court moved down the Festival Hall with a precise and ordered formality, which was yet entirely free from pomp and circumstance. It was indeed a company of learned men and women assembled to honour their chosen head. Doctors and scientists, lawyers, philosophers, and men of letters had laid aside their disputations to combine in a colourful pageantry in which black and scarlet predominated. The rectorial purple of Paris, side by side with the yellow and black of Strasbourg, mixed easily with the black gown and white ruff of Bologna, and hats of every description, from conventional velvets and mortar boards to the fez of Algiers and to others which could only be described as Churchillian, nodded together in dignified affability. Even royalty seemed to have shed much of its panoply when the Queen Mother in academic robes with a single page was escorted by the Chairman of Convocation down the centre of the hall and past the solitary Life Guard to her Chancellor's seat. There she assumed the responsibilities and gave the promises of her office, and in a gracious address reminded the assembly of a university's twin duties of teaching and research. She also congratulated London, already a pioneer in women's education, on the forward step it had taken by appointing its first woman Chancellor. She then invested the honorary graduates who were presented to her by the Public Orator with wit and scholarship. Musician, scholar, surgeon and statesman, a bishop with the common touch, an ambassadress and old opponent of the British Raj gifted with heaven-sent culinary skill, a distinguished Cecil honoured again after four hundred years by a Queen Elizabeth, all were welcomed to the catholic fellowship of the university. "Chancellor, I request you by the Authority of the Senate"...William Walton, Richard Livingstone, Malvern, John Wand, Vijaya Lakshmi Pandit, and Salisbury. The assembly stood for the National Anthem followed by the *Trumpet Voluntary* as the Chancellor departed for Guildhall. The ceremony, brief and inspiring as a spectacle, had given new meaning to the life and ideals of the university. Above all London had shown that its many and world-wide branches, despite their haphazard origin, had been united into a coherent whole. At last it had acquired a shape.

* * *

The derricks look on Rotherhithe, and Rotherhithe looks on the sea; and Fate having placed my hospital on the north, and my home on the south, bank of the Thames, I am obliged to plunge b.d. into the depths of the earth. The other day, dreaming there an hour alone—for my tube was as usual blocked—I thought of myself as a protein molecule driving an erythrocyte down a capillary in spasm. Other red cells before and behind (displaying anisocytosis and polychromasia) bore nutriments, reconstructive materials, and—yes—oxygen.

Towards the end of the second pipe-full, it was borne in upon me that this was a thrombosis rather than mere spasm, but as the half-hour approached I trickled turgidly towards the clot. Phagocytes were busy in their smart blue uniforms sorting out the particles, and a giant-cell trailing a thread of fibrin was dragging away the protoplasmic remains of an elderly and crenated red cell which seemed to be without its rear-wheels. Oh for an anastomosis! The wreck swung drunkenly at the end of its thread and the area threatened to slough, but I edged my erythrocyte smartly past towards the dim distant destination; and as I emerged into the blinding light I cried as with Beethoven's prisoners in *Fidelio*: "Oh welche Lust in freier Luft, den Athem Leicht zu Heben."

Rotherhithe Borough Council should, and doubtless does, realise that, as the fate of the world depends upon a few tiny arterioles in President Eisenhower, so does the integrity of their tunnel depend upon the tiniest grain of sand in any of the thousand and one carburettors which daily blow back and forth.

So when my dear Boss glowered at me from the end of the ward and asked, in his usual gentle way, what I thought I was playing at keeping him waiting for over an hour, he was surprised when I absently answered: "Studying pathology, Sir."

* * *

Acting as interpreter to some non-English-speaking colleagues during their visit to this country, I have become acutely aware of a new dimension of personality which operates whenever two or more people are striving to communicate with one another. This is the Individual Effector-Receptor Index, or more simply, E/R, which denotes a person's tendency to talk too much and to ask too many questions instead of listening to what is being said (= high E/R), or else his capacity to hear (= low E/R). When the discussion is between a person of high and a person of low E/R, or between people of low or medium E/R, interpreting is straightforward and meaningful communication is possible. When, however, the talkers both have high E ratings, the tensions set up are considerable, and the interpreter has to function mainly as a selective filter. Even so, at full working pressures, failure of effective communication is liable to occur, and the trouble is not, as is often supposed, a semantic one. The same thing happens in discussions between such people even when they are using the same language and there is no interpreter.

* * *

It was a medical outpatient clinic. Last week the patient had provided the subject for a demonstration to students on industrial pulmonary disease; we discussed a change of job and emphasised what a serious decision it was. We eventually favoured a change and the patient had now returned to report progress. Despite a thick yellow fog her chest had not so much as a whisper, she looked radiantly happy, quite different from the wheezing and anxious creature of last week. I could not help pointing out to the class how well she had done, leaving the inference of a wise decision to be drawn by the class.

As we finished and the patient left, Sister lent over and whispered "She tells me she has just won £500 on the pools."

* * *

He came in after the last patient had gone and sat in the consulting-room chair. "Doctor, it's my new Black Widows, I'm rather worried about them. I put them in with the Angels and now they've all come out in white spots."

We discussed icthyophthirius, and other protozoal diseases, their treatment by heating the aquarium to 80° or even 90°F, repeated once or twice to kill the spores, but eventually decided that an older remedy, quinine, should serve.

℞ Sol. Quinin. Hydrochlor. gr. 4 ad C. 1. Fiat Balneum pro piscibus.

* * *

When we admit surgical cases from the "cold" waiting-list we often have to ask the lady almoner to help with arrangements for dependants. But last week we had to consult our veterinary colleague.

"Dear Matron,

Thank you for your letter. I quite see your difficulty but I must try to come even if it is in the Winter as one leg has in this last fortnight become so painful and so should my turn come please will you let me know and providing the cow or the sow are not due and my Mother and the gardener are not ill and my ponies are all well I must come as I cannot now I feel put it off until June as my leg hurts so if I walk uphill and in May I hope to have my mare foaling and then I could never leave her. Thank you so much."

* * *

The patient had had a cholecystogram and a biligrafin test. When we asked him for his history, he said, "I came up to hospital and had a Billy Graham's test."

# Letters to the Editor

## ADRENOSPLENIC IMPLANT FOR HORMONE-DEPENDENT TUMOURS

SIR,—It is now evident that the combined operation of bilateral adrenalectomy and castration plays a small but useful part in the management of patients with metastatic, hormone-dependent tumours untreatable by any other means. Such tumours occur in carcinoma of the breast in women and in carcinoma of the prostate in men. Of the patients so treated, those who derive advantage from the total removal of their internal sources of sex hormones still require to be maintained indefinitely on cortisone. With this drawback in mind it occurred to me that if some adrenal tissue removed at operation were reimplanted into the patient's spleen, the liver might then inactivate any œstrogen or androgen, leaving the metabolic hormones relatively intact. The postoperative requirements of the patient for cortisone from external sources might then be very small indeed.

I understand that this concept is not new. With a similar aim in view, Galante and his group [1] in California have anastomosed the left adrenal vein to the splenic vein—a considerable technical achievement. This operation also runs the risk of failure either from thrombosis of the anastomotic channel on the one hand, or from revascularisation of the adrenal by branches of the systemic circulation on the other. Bernstein [2] has actually anticipated the present method by implanting the excised adrenals into the mesentery, a site which still leaves open a potential escape route for hormones into the systemic circulation by way of the mesenteric lymphatics.

The first patient to be treated by "adrenosplenic implant" was an elderly man with carcinoma of the prostate.

The operation was performed by Mr. F. R. Brown, the aftercare of the patient being in the hands of Dr. J. M. Stowers. On this occasion the first stage comprised castration and removal of the right adrenal, the more difficult side. Three weeks later the remaining (left) adrenal was removed through an anterior approach and 3–5 g. of glandular tissue was then implanted into the spleen by means of a small suprapubic trocar and cannula. A neatly fitting glass rod enabled the fragments of the gland to be deposited well inside the splenic pulp.

I am aware that the ovaries of rats [3] and mice [4 5] have been experimentally implanted into their spleens and that such ectopic ovaries occasionally become malignant. But the expectation of life of the patient with a metastatic, hormone-dependent tumour is normally so short that, for the present, the possibility of malignant transformation in the adrenal graft need hardly be considered. It remains to be seen whether the long-term results of adrenosplenic implantation justify the continuance of the method.

Department of Radiotherapy,
Royal Infirmary,
Dundee. JAMES F. RILEY.

## CŒLIAC DISEASE

SIR,—In his interesting and stimulating lecture which you published last week Dr. Sheldon quotes me as saying that "estimations of fæcal fat should be abandoned as evidence of steatorrhœa, both in diagnosis and in charting recovery."

As this is not what I said, and is the exact opposite of what I feel to be true, I should like to give my exact wording,[1] which was in the context of the value of fat balances versus other methods in the detection of steatorrhœa:

"Assessment of Fat Absorption. . . . It is extremely easy to measure fat in the fæces, but the only way of determining whether an abnormal amount is being excreted is by some form of balance. Unfortunately for many years past much good observational work has been largely wasted by the use of the microscopical appearance or estimation of percentage fat in the stool as a means of detecting defective fat absorption. Both these methods may be grossly misleading and neither of them is of any value as a quantitative index of the defect; although these examinations have their uses, they should be abandoned as evidence of steatorrhœa both in diagnosis and as indices of recovery."

The only way of obtaining evidence of steatorrhœa is, of course, the estimation of fæcal fat—but total fat and not as a percentage.

Department of Medicine,
University of Birmingham. J. M. FRENCH.

## HEROIN

SIR,—I find it deplorable that the Fellowship for Freedom in Medicine identifies itself with Dr. A. H. Douthwaite's resolution[2]:

"Believing that heroin is of the greatest value in the treatment of some medical conditions and that the ban on its manufacture would serve no useful purpose in this country or elsewhere, this meeting strongly urges the Home Secretary to reverse his decision prohibiting its manufacture for medical purposes."

I have practised medicine for thirty-five years and formerly used heroin. But long ago I came to the conclusion that there is no longer any indication for this habit-forming drug. When I joined the staff of this chest hospital over ten years ago, heroin linctus was in great demand. I introduced to this hospital dihydrocodeinone ('Dicodid'), which is much superior to codeine phosphate in its cough-suppressing effect; and heroin has disappeared from our prescriptions.

Holywood Hall Hospital,
Wolsingham, co. Durham. E. G. W. HOFFSTAEDT.

## URINARY STEROIDS AFTER PREDNISONE

SIR,—Professor Gray and his colleagues (Nov. 19) mention the presence of five steroid metabolites in the urine of patients treated with prednisone.

We have studied the metabolism of prednisone, both in man and in the adrenalectomised dog, and have regularly found seven steroid metabolites by the combination of various chromatographic techniques.

We have isolated prednisolone from the urine of patients treated with prednisone.[3]

Another compound appeared to be unchanged prednisone.

Two further compounds did not show U.V. absorption at 258 mμ but strongly reduced blue tetrazolium and had the same movement-rate as tetrahydrocortisone and tetrahydrohydrocortisone. Further identification is in progress.

Two more steroids show U.V. absorption at 258 mμ without yellow fluorescence after treatment with NaOH. They do not reduce blue tetrazolium, but give Zimmerman-reacting material after treatment with periodic acid.

Finally we found a steroid showing both U.V. absorption at 258 mμ and yellow fluorescence after NaOH treatment and reducing blue tetrazolium.

In some of the urines, but not in all, still other steroids were present.

Although not identical with Professor Gray's conclusions, our results confirm most of his views. But the finding of metabolites reducing blue tetrazolium without U.V. absorption suggests reduction of the $\Delta^4$-3-ketone as one of the metabolic pathways.

Internal Medicine Clinic,
State University,
Ghent, Belgium. A. VERMEULEN.

1. Galante, M., Rukes, M., Forsham, P. H., Wood, D. A., Bell, H. G. *Ann. Surg.* 1954, **140**, 502.
2. Bernstein, D. E. *Yearb. Endocr.* 1954-55, p. 370.
3. Biskind, M. S., Biskind, G. S. *Proc. Soc. exp. Biol., N.Y.* 1944, **55**, 176.
4. Li, M. H., Gardner, W. U. *Science*, 1947, **105**, 13.
5. Furth, J., Sobel, H. *J. nat. Cancer Inst.* 1947, **8**, 7.

1. *Proc. Nutr. Soc.* 1955, **14**, 33.
2. See *Lancet*, Nov. 12, 1955, p. 1030.
3. *J. clin. Endocrin.* (in the press).

## IN THE MENTAL HOSPITAL

SIR,—It is regrettable that the first two paragraphs of Dr. Houston's contribution last week to your "In the Mental Hospital" series should be so full of gross historical inaccuracies and fantastic misrepresentations. Such failings have not been absent from the other articles in this series, as your correspondence columns have indicated; and, in consequence, the whole series is losing much of its value in the minds of thoughtful and experienced readers.

The "lunacy reformer" with his very characteristic agitator's mentality has been a constantly recurring feature of British psychiatry for many years past. Your contributors cannot, for example, be ignorant of the excitements of the early 1920s when the "Montagu Lomax" agitation was at its height. Dr. Houston would, I am sure, be sorry and surprised to know that his opening paragraph is similar in provocative tone to that author's, though I am well aware that his motives and ideals are utterly different.

It is true that the paragraph can be read as though the malpractices he describes belonged to the past. He continues, however, to say "at last a new era is dawning and the doors of despair are being unlocked." He then proceeds to name certain excellent hospitals as leading the way in activities, most of which were flourishing vigorously in at least a majority of mental hospitals long before he was born.

I shall not burden your columns by giving detailed facts in support of that statement, which I could easily do; but I think it is a pity that such able and enthusiastic workers as Dr. Houston and his fellow contributors have not familiarised themselves better with the history of their specialty and with the work of the real reformers in it, to whom both patients and hospitals remain infinitely indebted.

London, W.1. HENRY YELLOWLEES.

## THE FORGOTTEN PATIENT

SIR,—On Nov. 12 and 26 you published comments on my articles on the Forgotten Patient (Oct. 29 and Nov. 5). These articles were based on a wide knowledge of mental hospitals in England and Scotland, and I am certain that the faults of which I wrote are not confined to a hospital here and a hospital there but are widespread. Of course, it would be a bad region which had to admit that everything I said applied to all its mental hospitals, but probably there are few psychiatrists who would not agree that some of my statements are true for one or other of the hospitals in which they have worked.

I will state the main reasons for which I wrote:

1. If things are wrong they should be corrected.
2. If bad things happen and are hidden, their occurrence should be made widely known.
3. A quiet acceptance of evils does little to ensure their termination.
4. The relations of a patient have the right to be told how he is treated and how he lives.

Turning to particular criticisms, I have no doubt that many old people with gross organic brain disease are improperly admitted to mental hospitals: in the usual good geriatric hospital they would overcome their restlessness within a few weeks. It is equally clear that many old people, whose psychotic illness or whose inadequacy in dealing with things has precipitated a breakdown in their confidence, are properly admitted to a mental hospital and are there restored to their normal health. Unfortunately they may not be equal to living alone in lodgings or flats and it is difficult to get anyone to accept a person from a mental hospital.

If the word "drove" is thought too picturesque, I will willingly substitute another; but this will not disguise the fact that large numbers of patients are improperly employed on hospital farms. On a farm the patient is not only out of sight but too often forgotten. He leaves the ward long before the doctor reaches it and only returns after the doctor has long since left it. By reason of his chronic illness and lack of initiative he is most unlikely to seek an interview with his doctor, and the latter may not seek one either. In theory he will be examined twice a year, but theory does not always agree with practice.

It is all very well for Mr. Sargood to speak so cheerfully about the work in his region. I too will say how good the good work is. But senior psychiatrists have willingly shown me bad things in their hospitals in the South West Metropolitan Region as they have done elsewhere. I am glad to hear that the majority of committee members perform their duties properly; but negligence does occur, though again I would prefer not to particularise.

Bracebridge Heath is fortunate to have so many Polish nurses and some Polish doctors; the opportunist will feel that this excellent staff for Poles might well solve the problem for all the mental hospitals in the Midlands! But how often does this obtain throughout the country? What of the hospital with three Poles, a Ukrainian, and a Yugoslav? How will they muster a doctor and a nurse for each nationality? Dr. Falla has argued from the particular to the general.

No-one will deny that neurotics are often severely disabled by their illness; but the ultimate test of disability is the necessity for inpatient care, which must surely never, or almost never, be essential for a neurotic. I should be pleased to know what valuable work for psychotics is being done by mental-health organisations. Is their work predominantly for the neurotic or the psychotic?

There can be no doubt that a great deal of effort is made in every mental hospital to treat the patients. What varies is the point at which this effort ceases. In a few it never ceases. In some it may be years before the psychiatrist decides he must devote his limited time (I dealt with this last year) to more promising material. But in many it stops the moment the patient leaves the admission ward; and in a few hospitals he never experiences any care because he is admitted straight to a chronic ward where no patient ever gets more than the most cursory attention. It is my contention that care ceases early rather than late.

Mr. Sargood implies that I employ half-truths and that my pictures are painted in lurid colours; Dr. Falla calls my descriptions exaggerated and distorted; Dr. Duncan says that what I say is grossly misleading. I do not think that there is any need to defend myself. No-one has to do more than travel a little to see for himself. The only difference between these critics and myself is in our interpretation of facts, and this interpretation ultimately depends upon the difference in our sense of values.

In the justified enthusiasm for the energetic treatment of recent admissions, one often hears the psychiatrist say what good work could be done for these patients if only he was not hampered by having to spend so much of his time looking after the chronic patients whom his predecessor had neglected. He will ask why these cannot be moved elsewhere and given the material necessities of life, so that he can, by his hard work on the present generation, prevent new admissions from ever becoming chronic. But, assuming that chronicity can be prevented by his energetic treatment—and I like to think that it can—this does nothing to solve our present problem, which is the restoration to health of the tens of thousands of chronic patients at present in our hospitals for whom the likelihood of a normal life seems remote indeed.

I think that most relations of chronic psychotics will share my beliefs; many psychiatrists evidently condemn them. The truth is most likely to come from the young nurse and the young psychiatrist. Miss Restell's letter

expresses admirably what all of us once felt before so many of our consciences became stilled by daily acquaintance with dreadful things, and before this made us accept the dreadful things not only as inevitable but also as correct.

De la Pole Hospital, Willerby, East Yorkshire. J. A. R. BICKFORD Consultant psychiatrist.

SIR,—Unable to claim professional qualifications, nor yet the authority of your correspondent the chairman of the Mental Health Committee of the South West Metropolitan Regional Hospital Board, with indeed no claim to speak save membership of two hospital management committees, I feel that someone must register a protest against the point of view expressed by Mr. Sargood in his letter last week. If the only lay people who have the opportunity to know the facts refrain from all but polite comment for fear of discouraging patients, it is hardly to be wondered at that the public at large are unaware that some 40% of hospital patients are ill fed, ill housed, and inadequately treated.

The asylum—or place of refuge—renamed mental hospital struggles against the handicaps of inadequate staff and equipment to justify the title of place of treatment. The mental health committee (like everyone else) does its best to help; but, as the *cri de cœur* at the end of the letter suggests, that help is limited, and the determination to maintain that all is for the best only sets in at board level.

The series of articles you are publishing will hasten a change of outlook which will save not only lives but also in time money—a matter that sometimes seems more important to administrators.

London, S.W.3. E. L. M. PULVERTAFT.

## FAT ABSORPTION

SIR,—We should like to draw attention to some inaccuracies in your report (Nov. 19) of our paper on the cellular phase of fat absorption presented to the British Society of Gastroenterology on Nov. 4.

Your report begins: "Dr. R. Schneider had fed unemulsified olive-oil to rats and had demonstrated that absorption took place despite the absence of bile and pancreatic lipase. The same was true of sodium oleate and liquid paraffin . . . ." This seems to imply that there was no evidence of emulsification with the two latter substances. We stressed, however, that under these conditions sodium oleate was converted in the intestine to a soap-stabilised oleic-acid emulsion and that liquid paraffin was administered in a pre-emulsified form; also that emulsification of the absorbed portion of olive-oil had most likely taken place. In short, the importance of emulsification in the process of fat absorption that we intended to emphasise was not mentioned in the report.

In line 9 your report says: "Olive-oil administered in fine emulsion passed into the lacteals . . . ." Olive-oil did this whether given as an emulsion or in the unemulsified state, and the possibility of spontaneous emulsification applies here as in the experiment mentioned above.

The report continues: "so did oleic acid, but not sodium oleate which needed these [upper-intestinal] juices for its absorption." We made no distinction between oleic acid administered as such and as sodium oleate, as the latter is converted in the intestine into the free acid. It is oleic acid that requires the presence of the upper-intestinal juices for its passage into the lymphatics whether administered as such or as sodium oleate.

In line 13 your report says: "Lipid, phospholipid, and fatty acid likewise passed into chyle." This statement contradicts the preceding sentence. "Lipid" is the generic term for all the substances under investigation, and oleic acid is a very important "fatty acid." In the previous sentence the different fate of different "lipids"—namely, of a triglyceride (olive-oil) and a fatty acid (oleic acid) was emphasised. Phospholipid was certainly estimated in the chyle, but the question of whether it had "passed into the chyle" was not discussed.

The remark: "These results were contrary to those found by Prof. A. C. Frazer in previous experiments" seems to indicate that this refers to all the points made in our paper. This is certainly not the case. The difference refers only to the experiments carried out with oleic-acid feeding in the presence of upper-intestinal juices—conditions under which one of the authors (Professor Frazer) found no evidence of a rise of lipids in lymph and peripheral blood in his experiments in 1943, whereas we did so in the experiments under discussion.

Department of Pharmacology, University of Birmingham. R. SCHNEIDER H. G. SAMMONS.

## A REPORT FROM HOSPITAL

SIR,—Can Dr. Fisher (Nov. 26, p. 1138) explain why the surgeon from whom he requested a report asked him "promptly and very courteously" to write for an official report to a "gentleman who appeared to be the administrative chief of the hospital?" I have asked a number of consultants what they would have done on receipt of a similar request, and they all said that provided there were no abnormal circumstances they would have replied direct.

Surely if any lesson at all is to be learnt from Dr. Fisher's story, it is that the surgeon to whom he made his request was at fault and not the lay administrator. Or have I perchance missed the point of Dr. Fisher's letter?

Manchester Victoria Memorial Jewish Hospital. M. GRUBER.

## MODIFIED ELECTROCONVULSION THERAPY

SIR,—We wish to reply to those who have commented on our article (Sept. 17).

We cannot agree with Dr. Fisher (Nov. 5) that there is no danger at all to life when straight E.C.T. is used, nor that the danger of bone complications is very small. Whatever one's personal experience may have been one cannot disregard the reported risks of straight E.C.T.—namely, a death-rate of 0·8%,[1] an incidence of vertebral compression fractures of 20·8% for males and 2·4% for females,[2] and an injury-rate of 2·4%.[3]

What does Dr. Tyndel (Oct. 15) mean by a "mere fraction" of bone complications in straight E.C.T.?

Both Dr. Fisher and Dr. Tyndel refer to an added or superimposed risk when a relaxant is employed alone with E.C.T. We should like to know what they think this risk might be when the small doses advocated by us are used. Far from believing that there is an added risk, we hold that the use of a relaxant alone in small doses eliminates the hazards in E.C.T. without imposing any new risk.

Dr. Russell and his colleagues (Oct. 15) advocate the 'Ectonus' technique. We believe that the prolonged tonus causes unavoidable cyanosis and at least the same degree of stress on the cardiovascular system as straight E.C.T. does. This stress is due to the Valsalva phenomenon. This phenomenon has been described as follows: "The Valsalva phenomenon results from increase of the intrathoracic pressure against a closed glottis; this impounds large amounts of venous blood in the extrathoracic large vessels. Upon the release of the Valsalva phenomenon at the end of an unmodified seizure, these large amounts of blood suddenly enter the heart, placing severe stress upon the heart musculature and the impulse conducting system."[4]

We should like to know what the fatality-rate was in a large series of cases treated by the ectonus technique.

With reference to Dr. Murphy's comments (Oct. 8), the number of cases that we reported was sufficient to give a statistically valid comparison of the three techniques. Moreover the technique we recommended has been employed as a routine treatment for several months in hundreds of cases in this hospital and has proved satisfactory. Dr. Murphy believes that the "proper administration of thiopentone and suxamethonium chloride is a safe procedure." We presume that he means that the treatment is given by an anæsthetist since it has been clearly stated[5] that the degree of safety with thiopentone is related to the special experience of the administrator. If one holds, as Dr. Murphy does, and as we do, that the use of straight E.C.T. is now unjustifiable, one must either use

1. Impastato, D. J., Almansi, R. *J. nerv. ment. Dis.* 1942, **96**, 395.
2. Kalinowsky, L. B., Hoch, P. H. Shock Treatments, Psychosurgery and other Somatic Treatments in Psychiatry. New York, 1952; p. 154.
3. Kelly, J. P. *J. Bone Jt Surg.* 1954, **36B**, 70.
4. *Confin. neurol. Basel.* 1953, **13**, 332.
5. Leading article, *Brit. med. J.* Oct. 1, 1955, p. 836.

a relaxant alone or use a relaxant and thiopentone only when an anæsthetist is present; the second of these two alternatives would impose an impossible condition on the administration of E.C.T.

We should like to emphasise that satisfactory modification is obtained with suxamethonium chloride ('Scoline') when the stimulus is given 10 seconds after the onset of facial fasciculation, and with suxethonium bromide ('Brevidil E') when the stimulus is given 3–5 seconds after the onset of facial fasciculation. If one waits for total paralysis, as Dr. Hewat and his collegaues (Nov. 5) have been doing, one subjects the patient to an unnecessary degree of anxiety without achieving any added benefit.

Middlewood Hospital, Sheffield. J. KELLEHER
R. W. WHITELEY.

## SECONDARY HÆMOCHROMATOSIS

SIR,—The demonstration by Dr. Davies (Nov. 19) that enough iron was administered by way of blood-transfusion to account for the increased amounts in the tissues of his patient with secondary hæmochromatosis is particularly interesting in view of conflicting reports on this subject.

I reached the same conclusion concerning a similar case,[1] and I observed that there was a correlation between the volume of blood given and the liver-iron content in 13 other patients who had received transfusion. No increase in liver iron storage was, however, found in 11 patients with chronic normocytic anæmia who had not been transfused, even though some of them had received oral iron.

Cases of secondary hæmochromatosis in which the tissue iron content is unaccountably high are exceptional, and their existence must not be allowed to obscure the fact that repeated blood-transfusion is the primary cause of this unusual condition.

Hammersmith Hospital, London, W.12. G. A. MACGREGOR.

## CONSULTANTS IN DERMATOLOGY

SIR,—Dermatology in this country is now recognised as an important branch of general medicine, and dermatologists must primarily be general physicians. One has only to remember that such conditions as disseminated lupus erythematosus, polyarteritis nodosa, sarcoidosis, and various reticuloses, first present with skin manifestations, to realise how important is this basic knowledge of general medicine.

The employment of underworked venereologists as dermatologists for administrative convenience is, as Dr. Ingram so rightly points out in his letter last week, a retrograde step in British medicine. If it is thought desirable for venereal disease to be treated by the physician interested in the organ affected principally by the disease, it is as reasonable for the condition to be treated by the cardiologist, neurologist, or genito-urinary surgeon as by the dermatologist. Conversely the training of a venereologist makes him no more of a dermatologist than, say, a cardiologist.

One further factor which depresses well-trained senior registrars (not only in dermatology, but in other branches of medicine) is the increasing tendency to advertise consultant appointments with only a few sessions. This is possibly justifiable in London, where it is probable that further sessions in other hospitals will be available, but in most provincial areas this is not the case and the appointment almost inevitably goes to the local candidate who can retain part of his previous appointment. Accordingly, consultant posts are being filled by applicants who are not necessarily the best available.

Sheffield. H. R. VICKERS.

1. *St. Thomas's Hosp. Rep.* 1950, **6**, 128.

## CARCINOMA OF THE BREAST

SIR,—I have noticed that the patient with carcinoma of the breast who is slow to regain normal health after operation is usually the one that develops early clinical secondaries. I know that experience, at least incomplete experience, is fallacious but this is all that anyone has. Excessive blood-loss, bigger operations, and postoperative complications all delay recovery, and must be avoided.

Recently it has been shown that smaller and more local operations give, in certain people's hands, better results than the classical modified Halstead, both procedures being followed by X-ray therapy. As I see it there are two possible explanations.

Hippocrates told us that operations on growths made them worse. This is very true—one should operate on normal tissues around the growth. If we believe that breast carcinoma usually spreads by lymphatic metastases rather than permeation, we have in an advanced case of carcinoma the primary in the breast, next a zone of normal tissue, and then glands in the axilla. If we carry out a local removal of breast we cut across the normal zone; if we conduct an axillary dissection we are in and around growth and so aggravate the condition, contravening Hippocrates's advice. Alternatively, in the smaller operation we have less blood-loss, fewer complications, and a quicker return to normal health. Of these two possibilities I think that the second is the more important factor, causing a better survival-rate; also the patient is much fitter when she receives her postoperative X rays. X rays seem to work not only by inhibiting the carcinoma cells, but also by producing local fibrous and other changes which imprison the carcinoma cells; and this, being a tissue-bed reaction, is more complete in the healthier person.

The cynic says that all patients after operation for carcinoma of the breast develop secondaries provided they live long enough. By this he infers that after operation he does not feel confident that he has removed all the carcinoma cells, and the cells left behind may become active at any time. Work on biopsies of retrosternal glands suggests that many cases of five-year cure have retrosternal deposits at the time of operation. Why are the cells that are left behind so often slow in producing a clinical secondary? Does removing the primary hinder the growth of the secondaries? This is seen in certain ovarian carcinomas where after removal of a primary observed secondaries disappear. It has been said that these secondaries are anyway of limited existence; but possibly the presence of the primary helps their growth—a hormonal control obvious in the ovaries but present in a lesser degree in all growths. That certain sites are more favourable for the growth of secondaries is well known—it may be that growth only becomes rapid should the cells move (this may be due to many causes) to a more suitable site. That trauma can liberate malignant cells is seen by the frequency with which operations at the site of a "healed" growth are followed by a recurrence.

The late development of a secondary in a case I saw when doing my first house-surgeon job impressed me greatly. Eighteen years after the excision of a primary carcinoma of a breast a rapidly growing secondary of the skin of the back appeared. What change had allowed the latent carcinoma cells to multiply? Trauma moving them to a new site, trauma stimulating their growth, or was it the result of some general systemic or glandular change? That the alteration of the general health of the patient does allow secondaries to grow is illustrated by the following case of mine.

A man with carcinoma of the tongue with secondary glands was treated by excision and block dissection. He remained without a recurrence for four years. I then operated on him because of a painful peptic ulcer. Six weeks after partial gastrectomy he developed a bloodstained pleural effusion that contained epidermal carcinoma cells. His lowered general condition apparently allowed the latent carcinoma cells to multiply.

I consider that there must be some factors in the patient's general health that inhibit the growth of secondaries, and submit that it is essential to ensure quick return to good health after operations on carcinoma. Radiotherapists, who see the day-to-day results of different surgeons, are aware that different surgeons get different results, although doing essentially the same operation. These differences depend, I believe, on the finer points of technique and care, and I submit the following rules for breast operations, all aimed at rapid postoperative return to health :

*Preoperative care.*—This is limited because delay is unwise. The patient should not be anæmic—blood-transfusion may be necessary. Full diet (calories and vitamins). Vitamin-C deficiency delays healing. Adequate rest with sedation if necessary to ensure sleep—the worry of a pending operation is distressing.

*Operative care.*—Premedication is given in relation to the anæsthetic. All effort must be made to diminish hæmorrhage ; clear airway and hypotension. There are many ways in which an anæsthetist can help diminish blood-loss. I think the importance of diminishing blood-loss possibly justifies hypotension. All blood-loss must be made up. The surgeon must pay particular care to save blood by meticulous hæmostasis. Clip before cutting. Clip the blood-vessel and the blood-vessel only ; no masses of tissue tied in the ligature so to die and create sepsis—clean cutting and no tearing. All that causes operative shock must be avoided. I myself carry out an axillary dissection unless there are fixed glands. Cutting through axillary growth is condemned. Postoperative œdema of the arm must not occur ; dissection into the arm lymphatic trunk is avoided—especially in obese patients, who tend to develop arm œdema. Closed drainage by a long tube is carried out and blood volume drained is charted. At all times the patient's hæmoglobin must be kept up. I feel that it is safer to leave skin than to delay healing by excessive removal. I prefer to skin-graft rather than to risk flaps sloughing. I prefer to cut a thick flap that does not die than to cut a flap too thin and risk a slough. Skin tension must be avoided.

*Postoperative care.*—This means good nursing, feeding, sleep, and avoidance or early treatment of any sepsis. I prefer the arm to be kept fully abducted and externally rotated ; early movement delays healing and causes lymph pooling. Postoperative X-ray therapy, should not be given till the patient is well, but should be given as early as possible. The healthy body aids the X rays in inhibiting the growth of neoplasm—mutis mutandis. The sooner the patient is fit the sooner the X-ray therapy can be given.

London Hospital, E.1. CHARLES HEANLEY.

## POLIOMYELITIS IN LONDON

SIR,—I rather think that Dr. Laurent (Nov. 19) has misunderstood me. It was the fact that in the majority of cases of so-called "abortive poliomyelitis" in North-West London, cell-counts of upwards of 100 in the cerebrospinal fluid without a single polymorph were the rule, that led to the suspicion that these cases were not poliomyelitis at all but some other virus infection of the central nervous system. Hence one's surprise to learn that in a certain—admittedly small—number of cases poliomyelitis virus (type 3) had been recovered. My own experience agrees entirely with Dr. Laurent's—namely, that in true paralytic poliomyelitis polymorphs always form a substantial percentage of the cells in the C.S.F., and sometimes the majority. It is not easy to understand why the same ratio should not apply in cases where no paralysis supervenes.

Dr. Laurent's remarks on the "peripheral" spread of the epidemic are very interesting. Broadly speaking one would say that the higher the standard of nutrition and environmental hygiene in a community, the more likely is epidemic poliomyelitis to occur. During the first epidemic in London in 1947, it was very striking to note how the cases clustered thickly among the better-class neighbourhoods, whereas in certain boroughs in the East End (Stepney, Poplar, &c.) they were relatively few. Perhaps the fact that standards are better in the suburbs may account for the curious track of the epidemic. Apart from that, however, in some instances there would almost seem to be a *genius loci* at work. If my memory serves, Lewisham in at least two epidemics has shown an unusually high incidence. I do not know it well enough to be in a position to assess its standards on the above basis ; but assuming both to be high, the incidence nevertheless still appears to be disproportionately heavy. Other localities have also shown similar patterns.

South Middlesex Hospital, Isleworth. G. E. BREEN.

## CONGENITAL AGAMMAGLOBULINÆMIA

SIR,—In your issue of Oct. 22 I described two cases of congenital agammaglobulinæmia occurring in brothers. In both, death was due to pneumonia of a peculiar type which I had not before encountered. Although the deaths of these two brothers were separated by an interval of almost five years, the histological appearances of the lungs were almost identical. After publication of my paper, Dr. H. S. Baar, pathologist to the Children's Hospital, Birmingham, wrote to me to suggest that in these brothers the lungs were infected with *Pneumocystis carinii*. Dr. Baar has kindly examined sections from the lungs of my cases and has confirmed that this was indeed the case.

While I understand that this protozoan infection is not uncommon on the Continent, only one publication has appeared in this country, by Dr. Baar himself.[1] The occurrence of this rare infection outside the European continent raises the question whether agammaglobulinæmia may not be a vital predisposing factor. The possibility obviously merits investigation.

I am grateful to Dr. Baar for having elucidated the nature of the fatal infection in my cases.

Royal Hospital for Sick Children, Glasgow, C.3. J. H. HUTCHISON.

## INFECTION ACQUIRED IN HOSPITAL

SIR,—A solution to the problem of hospital infection is urgently and universally needed. The recommendations enumerated below are effective and can mostly be implemented with existing equipment.

1. The M.R.C. rules for surgical dressings should be strictly observed.

2. Floors should be treated with substances that cause dust particles to adhere to the surface. Table-tops, ledges, shelves, &c., should be similarly treated. Dust can be still further subdued by the regular use of 'Microsol' sprayers containing dilute 'Hibitane' solution.

3. Infected dust collects in the interior of pillows and mattresses, which should be regularly disinfected in hot, moist, gaseous formalin in the hospital disinfector.

4. Blankets also collect dust. Before washing, blankets can also be disinfected in the hospital disinfector, using hot, moist, gaseous formalin. Washing blankets in 'Fixanol C' after treatment with a detergent to remove soap residues has a prolonged antibacterial effect on the blanket fibres.

5. Blankets, pillows, and mattresses can be protected by rubber or plastic envelopes : such a one is the 'Stannard' envelope for treating burns, supplied by the Milton company.

6. Clean surgical cases should be segregated. Open infectious cases should be isolated, preferably in cubicles, until free from infection.

7. Nurses should wear rubber gloves when handling infectious dressings or bedpans, and when changing babies' napkins, &c. The nurse can wash her gloved hands in soap and hot water and rinse her gloved hands in a solution of 'Milton' or other disinfectant.

8. All staff working in the wards should be gowned and masked.

If these rules are faithfully observed, antibiotic-resistant staphylococci and other organisms will cease to be harboured in hospitals.

St. Margaret's Hospital, Epping, Essex. FRANK MARSH
Director of Pathology.

1. Baar, H. S. *J. clin. Path.* 1955, 8, 19.

## WHO ARE THE INFECTORS?

SIR,—Your very important leading article last week on the unknown infector in tuberculosis calls attention to the need for seeking sources of infection as these diminish in number. No-one will disagree with your remarks about the necessity for intensification of preventive measures, which, as the epidemic of tuberculosis is nearing its close (largely, perhaps, from natural causes), should yield a bigger harvest than ever before. Routine chest radiography of certain occupational groups would undoubtedly help to quench foci of infection; but, unfortunately, the prospects of its widespread use in the near future appear remote. The public conscience in such matters needs a lot more stimulation before enough support can be obtained. Mass-radiography units, despite praiseworthy endeavour, have not been able to cast their nets widely enough in the most prolific fishing-grounds, where lurk the dangerous males in the older age-groups.

Fortunately chest radiography is not the only means available; tuberculin testing of young children has proved its worth in bringing to light the adult infector, as well as in discovering active disease among children themselves. This is being carried out to an increasing extent in child-welfare centres and schools, and meticulous inquiry by the doctor and health visitor very often discloses the source of infection of the positive reactor. The steady reduction in the percentage of reactors which has been noticeable during the past few years (an indication of the decrease in foci of infection) enables more time to be given to investigation than was possible a short time ago.

Nearly 17,000 children of pre-school age in this area have been tuberculin-tested at municipal clinics since 1947.† The jelly test was used in the majority of cases, but those who reacted were Mantoux-tested (about 5% proved negative); the net result over this period was a 1% conversion-rate. Whatever its shortcomings, the jelly test seems to err in the right direction. A number of the children were found to have active disease, but a greater number of adult infectors—previously known and unknown—were unearthed. These included the "lady next door," the nearby shopkeeper, and a clutch of uncles, aunts, and grandparents. Quite recently, tuberculin testing of children in a residential establishment, in which one of the staff was found to be tuberculous, resulted in the notification of eight cases in children.

The mass-miniature radiography unit has coöperated wholeheartedly in dealing with schools for older children in which one of the teachers has developed tuberculosis, but the yield has not been in proportion to the effort expended. Now, it is found that prior tuberculin testing is advantageous.

In assessing the rôle of tuberculin testing in the scheme of tuberculosis control, the cost is a factor of importance. It is computed [1] that under normal working arrangements of a mass-miniature radiography unit it costs just over £100 to discover an active case of tuberculosis. While no price is too high to pay for the draining of the unknown pool of infection, may it not be possible to reduce the expense by increasing use of tuberculin testing?

Town Hall, Camberwell, London, S.E.5. H. D. CHALKE.

## XERORADIOGRAPHY

SIR,—In an annotation (Nov. 19) you say of the xeroradiograph: "Its most striking difference from a conventional film is the presence of both bone and soft-tissue detail on the same plate."

This is a startling indictment of the modern radiograph, which in many cases, and often in the hands of skilled radiologists, is only a poor image of what it should be. All necessary bone detail can be produced by the right quality of negative with due reference to the surrounding soft-tissue structure, provided that the radiographic exposures and subsequent processing are correct. After well over thirty years' experience I am today frequently shocked by the radiographs presented to me of over-penetrated, over-exposed, and densely developed negatives which show "a bone" in a dark background.

The same remarks may well apply to abdominal radiographs, which are often grossly over-penetrated and which fail to show muscle shadows and other soft-tissue structures. In such radiographs many less opaque objects, such as renal or ureteric calculi, are often lost. Indeed, it would seem that modern radiography is concentrating too much on the "rare and occasional" demonstrated by marvellous variants of "-ography," to the detriment of straightforward photographic and radiographic principles.

London, W.1. F. M. ALLCHIN.

1. *Med. Offr*, Nov. 25, 1955, p. 308.

## RADIOTHERAPY CENTRE AT SHEFFIELD

Dr. W. A. RAMSAY, senior administrative medical officer of the Sheffield Regional Hospital Board, writes to correct the first statement in the news paragraph headed "Sheffield United Hospitals," on p. 1148 of our last issue. He informs us (1) that the responsibility for providing a new radiotherapy centre is that of the regional hospital board, which is at present trying to find a suitable site; and (2) that there has been no Ministerial approval of any plan to provide 60 new beds for radiotherapy in Sheffield. We are sorry to have misunderstood the situation.

# Parliament

## QUESTION TIME

### Guillebaud Report

Replying to a question, Mr. IAIN MACLEOD said that the Secretary of State for Scotland and he had now received the Guillebaud Committee's report on the cost of the National Health Service. Every priority was being given to printing it so that it might be in the hands of hon. Members at the earliest moment; but the document was voluminous (the summary alone covers more than 50 typescript pages), and he was afraid it must be some weeks before publication could take place. In the meantime, he was sure it would be improper for him to attempt either to summarise the report in his own words, or to comment on its recommendations. Although two members of the committee had made certain reservations—which would of course be printed with the report—the whole committee had signed the main report itself.

### The Death Penalty

Mr. SYDNEY SILVERMAN asked the Prime Minister, in view of the swing of public opinion in favour of the abolition of the death penalty, and of his refusal to grant time for the discussion of the Private Member's Bill introduced to give effect to this, what steps he proposed to take to ascertain the present stage of public opinion as to the death penalty.—Sir ANTHONY EDEN replied: I have no doubt that on this, as on other matters, public opinion will be able to express itself by the traditional means. We are prepared to consider providing time for a debate, but I am afraid that we cannot do so before Christmas, for fairly obvious reasons, having regard to the state of our programme, but I hope that we shall be able to do so very soon after our reassembly.

### Ban on Heroin

Replying to a question, Mr. MACLEOD said that the Medical Advisory Committee which advised him concerning the ban on heroin was appointed under statute and included the presidents of the three Royal Colleges, the chairman of the council of the British Medical Association, the president of the General Medical Council, and the chairman of the council of the Society of Medical Officers of Health. It also included four consultant physicians, five consultant surgeons, and five general medical practitioners, all of whom were appointed after consulting the appropriate medical organisations.

### Industrial Hazards

Replying to a question, Sir WALTER MONCKTON, Minister of Labour, said the Industrial Health Advisory Committee had recommended the stimulation of voluntary medical supervision in the steel foundry, iron and steel manufacturing, rubber, and chemical industries.

### Industrial Dermatitis

Dr. BARNETT STROSS asked if the Minister was aware that many employers and workers still mistakenly believed that industrial dermatitis was contagious; if he was satisfied that the officers in employment exchanges were fully aware that there was no such possibility of infection; and what steps would be taken in the campaign against dermatitis.—Sir WALTER MONCKTON replied: I am aware that misapprehensions about industrial dermatitis may still exist among some employers and workers although the position is made clear in a poster issued by my Factory Department. I am satisfied that the officers concerned in employment exchanges with persons disabled by dermatitis are aware of the facts. The Chief Inspector of Factories has revised and reissued a leaflet and a poster containing advice on prevention, and further measures to stimulate the interest of employers and workers in the need for precautions are now under consideration. Special visits are paid to factories where dermatitis is known to be a problem and inquiries are being made into the risk of dermatitis from certain substances. Attention is also being paid to the problem in the course of the pilot local industrial health survey now in progress in Halifax.

### Lighter Hearing-aid Batteries

Replying to a question, Mr. MACLEOD, Minister of Health, said that the Mark III hearing-aid, with batteries about half the weight of those for earlier models, was available in all parts of the country and was issued to patients who needed it. An even lighter monopack model had just passed its clinical field trials and would, he hoped, be available for distribution to children in about a year's time.

### Medical Inspectors of Factories

Replying to a question, Mr. HAROLD WATKINSON, parliamentary secretary to the Ministry of Labour, said that the medical inspectors of factories numbered 13 in 1951, and were the same number now. 2 more would shortly be joining the department from the recent open competition. It was hoped to recruit a further 3.

### Rabies

Replying to a question, Mr. HEATHCOAT AMORY, Minister of Agriculture, said that 1949 was the last year in which it was reported that one or more dogs brought into Britain had developed rabies during or after quarantine. Replying to a further question, Mr. MACLEOD, Minister of Health, said he understood that in man the disease was invariably fatal. In 1947 there was one death from this cause, and the next had occurred this year.

### Increased Cost to N.H.S.

Replying to a question, Mr. MACLEOD said that the increased cost to the National Health Service of the proposed increased taxation was about £1 million a year.

## Public Health

### An Unidentified Illness

OF 190 children at the county secondary modern school, at Tottington, Lancashire, 63 (24 boys and 39 girls) have lately been affected by an illness so far unidentified. The chief symptoms were headache, dizziness, nausea, and slight abdominal pain.

In a typical case, a girl of 12 complained of slight dizziness and pain at the back of the head. Later her legs felt numb, as if walking on air, and her vision was blurred. There was sharp abdominal pain across the umbilicus. Pulse-rate was 66 and temperature 99°F. A number of the children affected had slow pulse-rates of 65–70 and temperatures ranging from 97° to 99·5°F.

Similar cases appeared in all parts of the school at different times of day over a period of four days. The children recovered quickly and returned to school after one or two days' absence. Moderately dilated pupils were noted in several cases. A local doctor said he had a similar illness the previous weekend and that 5 adults were similarly affected in his practice. The other 2 local doctors had nothing abnormal to report. Throat washings were put in broth for virus examination, and blood and fæces samples were taken from 6 cases.

On the fourth day there was a further batch of cases, including one child severely affected.

A girl of 11 had sore throat, dizziness, and pains in the stomach and top of the legs. At 10.30 A.M. next day, felt faint. Fainted at 11.30, after being removed from classroom to another part of the school with open doors and windows. Slight cyanosis, legs rigid, closed eyelids fluttered, conscious about 12.45. Corneal reflexes present during unconsciousness, but she could not be roused. At 1.15 she was quite bright and cheerful, good colour. At 2 P.M. pulse 126, temperature 98·6°F.

Analysis of the 46 cases during the first few days enabled school meals, milk, and water-supplies to be excluded as a cause.

The weekend followed and there was almost 100% attendance on Monday morning. The first child collapsed about 9.45 A.M. and others went down all day in different classrooms all over the school. 19 of them were children who had collapsed the week before. A number became restless with intermittent periods of unconsciousness; the pupils were dilated, and the corneal reflex was present, but the children could not be roused. A new symptom was dryness of the mouth. Children collapsed long after they had been removed from their classrooms to the domestic flat in the school where the doors and windows were wide open.

No child was so continuously ill as to require hospital treatment but a child who had collapsed twice was sent to hospital for examination. Nothing abnormal was found except a temperature of 99·6°F. Spectroscopic examination of the blood was negative for carboxyhæmoglobin. 3 other children who relapsed at a later date in a cinema (probably with poor ventilation) were also sent to outpatients and again spectroscopic and routine examination of the blood was negative. The urine was normal.

It was decided to close the school and to look for some form of gaseous poisoning. Attention was directed to the assembly hall where a number of children had collapsed during a singing lesson and which was the only place where all the pupils congregated.

Beneath the stage in the hall in a warm cellar were 40 sacks of floor-sweeping compound which gave off a strong chemical smell. These were analysed with negative results: the smell was pine oil plus wood shavings. It was then discovered that the sacks were second-hand and had contained fertilisers, apparently nitro-chalk. No volatile organic compounds were obtained from the sacks, and tests were negative for organic phosphorus compounds. There were also several large canisters of a floor cleaner—sodium carbonate and metapyrophosphate. In addition there were sealed 5-gallon cans of a wax floor-polish containing di-ethanol amine, olein emulsifier, and various waxes. All these were taken to a distant unheated building. The wax floor-polish had not been applied for two months. There were no leaking fire extinguishers, and in any case they did not contain methyl bromide.

There was no smell of coke or boiler fumes, but a trap-door from the side of the stage led to the cellar and thence by passages direct to the boiler-house. It was possible for any boiler fumes to travel along the heating pipes which ran under the corridors. A panel was removed from a duct carrying heating pipes at the side of the stage and after an hour or two a smoke haze was noticed in the hall. No carbon monoxide was detected by the diagnostic-tube method. The test was repeated with the heat full on and all windows closed. Results were entirely negative. On one occasion, however, a considerable escape of boiler fumes was observed from the base of one automatic hopper and this lasted a few minutes. The fumes were not pungent and would not be noticeable apart from the smoke which would settle out. If this were repeated at regular intervals during the night when the boilers were damped down, no doubt fumes could reach the assembly hall and some of the heating ducts. The boiler attendant said he had not had trouble with back draught, but the weather during the week in question was foggy with temperature inversion. There was very little fog in the vicinity of the school. The boiler chimney was also very low and not much above the level of the hall.

Fumes would have to travel to distant classrooms in order to explain the collapse of pupils several hours after they had left the assembly hall. One of the first cases was a child who had not entered the assembly hall. No-one complained of fumes or even noticed any. One teacher was slightly ill; the staff may have been pro-

tected in the assembly hall because they sat on a higher level and there was a down draught from the roof on to the stage.

The school reopened on Monday of this week, and 21 children complained of slight dizziness; but they had almost all been ill earlier in the outbreak and none of them was severely affected on returning to school. Up to midday on Tuesday, nothing further untoward had been reported.

At first a virus infection was suspected, but the recurrence of symptoms in 19 children after the week-end was against this. On the other hand, a virus is suggested by the fact that apparently similar outbreaks have been reported at West Hartlepool, co. Durham, on Nov. 8 and 9 and at Lincoln on Nov. 23. At present the most likely cause seems to be a poisonous gas affecting the central nervous system. Carbon monoxide seems to have been excluded, but a less well-known poison, such as methyl bromide, might be acting in low dilution and producing delayed effects. Methyl bromide is a heavy gas and would affect children before adults. But no source has yet been discovered.

For this account of the outbreak, we are indebted to Dr. C. H. T. Wade, divisional medical officer, Lancashire County Council, who has been making these inquiries in consultation with Dr. S. C. Gawne, county school medical officer, and Dr. M. T. Parker, of the Public Health Laboratory, Manchester.

## Typhoid Fever in London

In London 11 cases of typhoid fever have been confirmed in Polish residents of Westminster, Hampstead, Fulham, Kensington, and Acton. Almost all those affected went to a party given by a Polish lady in Acton on Oct. 15. The first patient fell ill on Oct. 21. So far as possible, a list has been compiled of the guests at the party, but this may not be entirely complete; so it is possible that untraced guests may be infected and as yet undiagnosed. Unexplained pyrexial illnesses in the London area, especially in Polish people, should be considered with these facts in mind.

## Poliomyelitis Vaccination

At a W.H.O. conference in Stockholm last week,[1] it was reported that results from the five countries already using the Salk type of poliomyelitis vaccine showed a good degree of protection among the age-group in which it was used. The general feeling was that, when properly manufactured and tested for safety, the Salk type of vaccine was as safe as any of the vaccines used against other diseases. It was agreed that the potentially dangerous Mahoney strain of type-1 virus used in the Salk vaccine should preferably be replaced by a safer strain. Dr. Albert Sabin said that with a little work a strain could soon be produced which would be as effective antigenically as the Mahoney strain without any of the attendant risk.

Figures were given [2] for some of the results of vaccination in the United States, Canada, and Denmark.

Of 450,000 children aged 6 to 10 who were vaccinated in New York State, 153 contracted poliomyelitis, 18 with paralysis. This paralysis rate of 4 per 100,000 compared with 21 per 100,000 in the unvaccinated control group of 260,000. In Minnesota, 3 out of 112,000 vaccinated children were paralysed, whereas 10 paralytic cases occurred in 33,000 unvaccinated controls. In Canada, where 860,000 children aged 5 to 9 were given a similar vaccine, preliminary results showed a paralysis rate of 1·07 per 100,000 vaccinated, against 5·39 per 100,000 unvaccinated. In Denmark no case of poliomyelitis had been reported among 425,000 children vaccinated in April, but there have been only 7 cases among the whole population since then.

There has been a further fall in the number of poliomyelitis notifications in England and Wales. Total uncorrected notifications for the week ending Nov. 19 were (previous week in parentheses): paralytic 111 (127), non-paralytic 63 (99), total 174 (226).

1. *Manchester Guardian*, Nov. 29, 1955.
2. *Times*, Nov. 24, 1955.

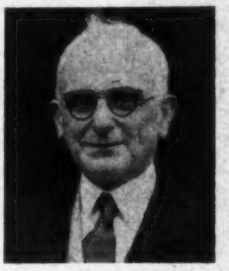
# Obituary

## WILLIAM ROBERTSON SNODGRASS

M.A., M.D., B.Sc. Glasg., F.R.F.P.S.

Dr. Snodgrass, a former president of the Royal Faculty of Physicians and Surgeons, died in Glasgow on Nov. 22, at the age of 65.

His father was a much-loved Glasgow general practitioner. William Snodgrass was educated at Glasgow Academy and Morrison's Academy, Crieff, where he was dux. At Glasgow University he graduated successively in arts, science, and medicine, taking his M.B. in 1913. He was house-physician to Prof. W. K. Hunter in the Glasgow Royal Infirmary before he left to serve throughout the 1914–18 war with the R.A.M.C. On his return from France he was appointed to the staff of the Western Infirmary in 1919, an association which remained unbroken until he retired under the age-limit eight weeks ago. At first he was assistant to Dr. R. Barclay Ness, who greatly influenced his formative years. Later he worked with Dr. George Allan, who roused his special interest in cardiology.



*Northern Press Photo Agency*

He had graduated to consulting work through general practice, and he always held that this was a most valuable part of the training of any young physician. In his early days he turned to the treatment of venereal disease, at first in order to augment his income. However, he became fascinated by research in syphilis, and the thesis for which in 1935 he was awarded the M.D. with honours and the Bellahouston gold medal was based on this work. It was summarised in publications in the *Quarterly Journal of Medicine* and by the Medical Research Council. Later he shared in M.R.C. therapeutic trials and wrote on the early results of sulphonamide therapy. He was the first to use penicillin in the Western Infirmary. As his ability as a general physician became recognised, he gave up his venereal-disease work and soon built up a large consulting practice in general medicine. He was appointed visiting physician to the infirmaries of Kilmarnock and Dumfries, to the Garrick Hospital, Stranraer, and to the Glasgow Eye Infirmary. As physician to the Southern General Hospital, Glasgow, he did great work in helping to transform a poor-law institution into a large first-class general hospital. In 1942 he was appointed consultant physician in charge of wards at the Western Infirmary, and there many of his happiest hours were spent in the hospital of which he had become so fond.

Dr. Snodgrass was proud of his long association with the Royal Faculty of Physicians and Surgeons of Glasgow, of which he became a fellow in 1920. He served the Faculty loyally on many committees and was honorary librarian from 1933 to 1946. In 1947 he was elected visitor, and he was president from 1948 to 1950, during the celebration of the 350th anniversary of its foundation. He represented it on the Joint Consultants Committee and devoted much time and energy to negotiation during the difficult early days of the National Health Service. But even the wear and tear of committees could not smother his sense of duty or his sense of fun, as his lines On *The Committee Man* [1] show:

> "I've tried all the trains and I hate all the lot, from the 10.25 to the 1 o'clock Scot.
> I'm fed-up; I'm finished: I feel that I ought to work quietly at home but I'm off like a shot,
> And I travel all over again."

His pen took easily to verse, and when we once unwittingly took his name in vain he sent a neat parody warning us that "All the Snodgrasses are over the border."

He served the University of Glasgow both on committees and as an honorary clinical lecturer. J. D. O. K. describes how a crowd of breathless lads and lasses were

1. *Lancet*, 1950, ii, 304.

to be seen running up the stairs in the Western Infirmary on the first day of enrolment for clinical classes.

"Members of the XV were thought by their colleagues to possess unfair advantages in the scrimmage to secure one of the coveted places in Snoddy's class. They loved him and he loved teaching them, and was curiously touched when they wished to entertain him to dinner at the end of the session.

"He was full of the vital spark which inspired his juniors to work for him and his patients with fanatical devotion; his was a life full of colour—reds and purples often. He did not bear fools gladly, but he had ample generosity to find time to listen to those, and there were many, who sought his guidance. As an opponent he fought cleanly and without malice. The only thing of which he was completely intolerant was intellectual dishonesty. But those who met him as a public figure or as a colleague on committees did not know the real man. Only those who had seen him with hospital patients, gently endeavouring to aid the bad home circumstances which had led to admission, understood his infinite capacity for taking pains. Only those who saw his constant compassion for desperate illness knew the true gentleness of this great physician. Only those who saw his wonderful way with a frightened child knew the true simplicity of his nature. Only the few who realised the difficulties of his last year knew the full heights of his courage."

S. A. writes:

"If ever a man was a bonny fechter that man was William Snodgrass. He was a man with objectives and ideals and he left his mark on all that he touched. But medicine in its turn moulded his character: the son of a physician who follows in his father's footsteps is exposed all his life to influences at once powerful and benign. Snoddie's magnificent independence was only an outcrop from a personality which was ever thoughtful and kindly. His was the spirit of the crusader, ruggedly independent even to the point of austerity. As might be expected, his teaching at the bedside was vigorous, challenging, and dogmatic; to be one of Snoddie's students was a rewarding if chastening experience. But he had a pawky sense of humour; and when he laughed he was changed in the twinkling of an eye to a mischievous schoolboy. In an imperfect world his passion for intellectual honesty and fair dealing were not calculated to make for peace of mind; yet his courage never failed, nor did his deep sense of chivalry. This same firmness of character was a tower of strength to his patients and an inspiration to his friends: he gave freely from a rich store of experience and culture. It was his lot to 'feel the heart-break in the heart of things,' for his wife died only a few weeks ago. The loss was irreparable: it was she above all who sustained him by her gentleness, her equanimity, and her profound understanding of this tempestuous but lovable character."

Dr. Snodgrass is survived by two daughters.

## HAROLD PACE GIBB

M.B. Camb., F.R.C.S.

Mr. H. P. Gibb, surgeon to the Central London Ophthalmic Hospital, who died at Gerrard's Cross on Nov. 21 at the age of 77, received his medical training at the University of Cambridge and St. Bartholomew's Hospital. After qualifying in 1904 he went on to take the F.R.C.S. in 1906 and the M.B. Camb. in 1907. J. H. P. writes: "He was a man of so retiring a disposition that his outstanding ability was known to only a few. He was my clinical assistant at Moorfields for several years, coming to me with an established reputation as a neurologist, won as a house-physician at Queen Square. He soon gained an equally high reputation as an ophthalmologist. He took little interest in private practice, but devoted himself wholeheartedly to hospital practice, winning the warm affection of his patients. During the whole of the late war he did most of the work at the Central London Ophthalmic Hospital, which was depleted of the younger members of its staff. He was a brilliant clinician, and it was a matter of regret to me that he did not write a book on the neurological aspects of ophthalmology. No-one was better qualified to do so. He had many interests outside medicine—art, sport, and literature. He was a friend whom I valued very highly; and it has always been a regret to me that he did not attain that wider recognition to which his intellect and character entitled him."

# Notes and News

## EXCITING RETURNS

WITH experience, the Nuffield Foundation are spending more money on more things.[1] Last year they distributed £681,400 which is almost three times as much as their first allocation of £248,600 in 1943. The increase has allowed them to extend their interest from workers and students in the United Kingdom to those in the Commonwealth. The Foundation consider this side of their work both important and rewarding, and over the past twelve years they have allocated over £1 million to travelling and research grants and other projects overseas. But expansion abroad has not meant retrenchment at home, and the Foundation has continued to offer stimulating and constructive help to research in this country. Their total grant to medical research, for instance, now stands at £875,000 (including £295,000 for rheumatism), for biological research at £586,000, for projects in social sciences at £684,000, for the care of the elderly and research into ageing at £970,000.

Till this year in their reports the Foundation have only been able to tell us of promising research or interesting enterprises which they thought worth backing. This year they are able to lead in the first of their winners. Mrs. Dorothy Hodgkin, F.R.S., and her team at Cambridge have elucidated the structure of the molecule of vitamin $B_{12}$.[2] Last year, maintaining the Camford balance, Dr. Macfarlane and his colleagues at Oxford described a method of extracting anti-hæmophilic globulin from ox and pig blood.[3] As a clinical report in our columns [4] last week shows, this work has already proved its value in the surgical treatment of hæmophilic patients.

New grants, which may well add to the interest of future reports of the Foundation, include: £15,000 to the University of Oxford for research under the direction of Dr. Honor Smith into immunological reactions of the nervous system; some £35,000 to Frenchay Hospital for Dr. R. M. Norman's research into causes of mental deficiency; and £8000 to St. Bartholomew's Hospital for Prof. K. J. Franklin's research into the physiology of ageing from conception to death.

## RESEARCH ON CHILD DEVELOPMENT

THE second annual meeting, organised by the International Children's Centre, Paris, of the research teams collaborating in studies of child development, was held in Stockholm on Oct. 10 and 11 under the chairmanship of Prof. Arvid Wallgren (Stockholm). Dr. Frank Falkner and Dr. C. B. Hindley, of the Child Study Centre of the Institutes of Education and Child Health, attended on behalf of the London team, and teams from Brussels, Dakar, Paris, Stockholm, and Zürich also sent representatives. All are conducting long-term follow-up (longitudinal) studies of physical and mental development.

The meeting carried forward the work, begun in Paris in 1954, of developing a minimum "base-line" of techniques, to be used at all the centres. The agreed methods cover such aspects as socio-economic data, anthropometric measurements, the clinical examination of the child, and the use of the same psychological tests and psychological-interview procedures. This collaboration should enable workers not only to confirm the findings of other centres, but also to compare the development of children in European countries and those living in more primitive communities.

## DISCHARGE AND READMISSION

IN his articles in our series "In the Mental Hospital," Dr. J. A. R. Bickford [5] said that "the sheltering of patients in hospital without continual efforts to make them fit to return to the world is a complete denial of the functions of medicine." Though there is, of course, no point in discharging patients merely for the sake of discharging them, the psychiatrist should regard discharge as his objective and must accept the fact that "a proportion of those he discharges will inevitably require readmission within a few months."

Some valuable data on readmission are given in the latest report from Graylingwell,[6] in which Dr. Joshua Carse, the

1. Nuffield Foundation Report 1954–55. Nuffield Lodge, Regent's Park, London, N.W.1. Pp. 125.
2. See *Lancet*, Oct. 1, 1955, p. 710.
3. Macfarlane, R. G., Biggs, R., Bidwell, E. *Ibid*, 1954, 1, 1316.
4. Fraenkel, G. J., Honey, G. E. *Ibid*, Nov. 26, 1955, p. 1117.
5. *Ibid*, Oct. 29, 1955, p. 917; Nov. 5, 1955, p. 969.
6. 58th Annual Report of Graylingwell Hospital, Chichester.

medical superintendent, records a follow-up of 584 patients discharged in 1949. Of these, 416 remained out of hospital for the following five years, and of the 168 readmitted, 100 required only one further period of treatment in hospital. Rather more than a quarter of those discharged in 1949, therefore, needed further inpatient treatment; but, as Dr. Carse remarks, "many thousands of people subject to attacks of gout, rheumatism, bronchitis, hay-fever, asthma—to mention only a few conditions—would be overjoyed to learn that following treatment nearly three-quarters of them could expect to remain free from attack during the next five years."

The depressions and schizophrenia account for most of the readmissions: of the 209 with depressions who were discharged, 66 were readmitted, and of the 129 schizophrenics, 46 went back to the hospital. Dr. Carse emphasises the need for more research into prevention, treatment, and aftercare in mental disorders, especially the depressions of middle-aged and elderly women.

## CORTISONE AND HYDROCORTISONE PREPARATIONS

THE Ministry of Health is informed that the prices of cortisone preparations at present available are as set out in the list below. This gives the basic price. The cost of an actual prescription is increased by the addition of 25% on-cost, as well as a dispensing fee and container allowance.

| *Name* | *Strength* | *Pack size* | *Basic price* |
|---|---|---|---|
| *Cortisone acetate* | | | |
| Eye-drops .. | 1% suspension | 3 ml. dropper bottle | 3*s.* |
| Eye ointment .. | 1% | 3 gramme tube | 2*s.* 6*d.* |
| Injection .. | 25 mg. per ml. | 10 ml. vial | 11*s.* 3*d.* |
| Tablets .. .. | 5 mg. | 20 tablets | 5*s.* |
| | | 50 tablets | 10*s.* 6*d.* |
| | 25 mg. | 20 tablets | 17*s.* 6*d.* |
| | | 40 tablets | 35*s.* |
| | | 100 tablets | 86*s.* |
| *Hydrocortisone free alcohol* | | | |
| Skin lotion .. | 0·5% | 20 ml. plastic bottle | 9*s.* |
| | 1% | 20 ml. plastic bottle | 16*s.* |
| Tablets .. .. | 10 mg. | 25 tablets | 15*s.* |
| | | 100 tablets | 56*s.* 3*d.* |
| | 20 mg. | 20 tablets | 24*s.* |
| | | 25 tablets | 30*s.* |
| | | 100 tablets | 112*s.* 6*d.* |
| Solution for use with intravenous drips | 5 mg. per ml. | 20 ml. container | 11*s.* 9*d.* |
| *Hydrocortisone acetate* | | | |
| Eye-drops .. | 1% | 3 ml. dropper bottle | 4*s.* 6*d.* |
| Eye ointment .. | 0·5% | 3 g. tube | 3*s.* |
| | 2·5% | 3 g. tube | 8*s.* |
| Injection .. | 25 mg./ml. | 1 ml. vial | 3*s.* 1*d.* |
| | | 5 ml. vial | 10*s.* 6*d.* |
| Skin ointment .. | Non-greasy and greasy 1% | 5 g. tube | 5*s.* 3*d.* |
| | | 15 g. tube | 13*s.* 3*d.* |
| | | 20 g. tube | 16*s.* |
| | Non-greasy and greasy 2·5% | 5 g. tube | 12*s.* |
| | | 15 g. tube | 29*s.* 6*d.* |
| | | 20 g. tube | 36*s.* |

## MEDICAL RESEARCH IN EIRE

NEWS of further research into the chemotherapy of tuberculosis is contained in the report for 1954 of the Medical Research Council of Ireland.[1] A compound synthesised in the laboratories of Trinity College, Dublin—1-salicylidene-2-isonicotinoyl hydrazine ('Salizid')—has been released for clinical trials in the United States. The drug is said to be as effective, dose for dose, as isoniazid, but to be free from undesirable side-effects. After nine months, 27 patients treated with salizid had an average gain in weight of 22 lb.; nearly all of them showed radiographic improvement; and the sputum of half of them had become free of tubercle bacilli. Early results of clinical trials in Dublin of 'Hisconstarch,' an oxypolysaccharide polymer, are said to be most encouraging.

Hypochromic anæmia was found in 31·4% of 1000 pregnant women in the Coombe district of Dublin; a survey of 504 of these patients indicated that in many cases diet and housing conditions alone were not responsible for the anæmia. 8 cases of megaloblastic anæmia were found in 3000 antenatal patients—a ratio of 1 in 375.

The ratio of female to male anencephalics in 12,552 births in three Dublin maternity hospitals was 8 to 1; this is much higher than the usually accepted ratio of 3 to 1, and more detailed study is proceeding.

1. Published by the council, 50, Merrion Square, Dublin.

The prevalence of rickets in Dublin in 1954 has declined notably: of 1000 aged from 3 months to 4 years, 3 had the disease in 1954, compared with 70 per 1000 in 1948.

## MEDICAL WAR RELIEF FUND

THE committee of this fund, at a meeting in London on Nov. 10, approved a report prepared by the distribution subcommittee. In the year 1954–55, seventeen educational grants, amounting to £1451, and twelve maintenance grants, totalling £1263, had been made. In addition, three special gifts, amounting to £90, and one loan of £100 were approved. There were no new applications for help during the year. At Aug. 31 the balance remaining in the fund was £7486.

## University of Oxford

On Nov. 19 the degree of D.M. was conferred on K. B. Taylor.

## University of London

On Oct. 19 the following degrees were conferred:

*M.D.*—G. T. Johnson.
*M.S.*—F. T. Graves, J. P. Mitchell, G. W. Taylor.

At a recent examination for the academic postgraduate diploma in psychological medicine Philip Haden and S. G. E. Laverty were successful.

## University of St. Andrews

Dr. William Walker has been appointed lecturer (grade I) in therapeutics at Queen's College, Dundee. Associated with the post is an appointment as honorary assistant physician (consultant) at Maryfield Hospital. Mr. W. F. Walker has been appointed lecturer (grade I) in surgery and will hold, along with his lectureship, an appointment as honorary assistant surgeon (consultant) at the Dundee Royal Infirmary. Mr. A. Buchan, consultant in midwifery and gynæcology, and Dr. J. S. Frew, consultant in therapeutics, have been appointed honorary lecturers.

## Royal College of Surgeons in Ireland

On Nov. 18 T. K. Jones and R. W. Poole were admitted to the fellowship.

## Institute of Almoners

The annual general meeting of the institute is to be held on Friday, Dec. 9, at 6 P.M., at the Royal College of Surgeons of England, Lincoln's Inn Fields, London, W.C.2, when Sir David Lindsay Keir, the Master of Balliol, will speak on the Art and Science of Being an Almoner.

## Heberden Society

At this society's annual dinner in London on Nov. 25, Mr. Leslie Farrer-Brown remarked that in the past twelve years great strides have been made in the attack on rheumatism. There were now more well-staffed and well-equipped research centres; and controlled trials had cleared the ground for further progress. Mr. Farrer-Brown was proposing The Society; and in his reply Dr. J. V. Wilson spoke with pride of the society's high standard. There now exists, he declared, the organisation for research, and the society can offer the necessary leadership. The Guests were toasted by Prof. R. E. Tunbridge, the president, who spoke of Lord Nuffield's philanthropy, with special reference to advances in knowledge of rheumatism that he had made possible. Professor Tunbridge went on to speak of the good quality, and the prosperity, of the society's official journal, the *Annals of the Rheumatic Diseases* (founded by the Empire Rheumatism Council); and he acknowledged the important contribution to this success of Dr. Hugh Clegg, Editor of the *British Medical Journal*, who is on the editorial board of the *Annals*. Sir Hubert Houldsworth and Lord Nuffield responded for the Guests. Lord Nuffield remarked that his aim had been to encourage work on diseases that disable but do not usually kill—for instance, rheumatic and orthopædic disorders. But he had also sought to promote progress in other fields that he regarded as neglected—namely, anæsthetics and obstetrics and gynæcology.

The evening was marked by a lively exchange concerning relations between Harrogate and the city of Leeds. Dr. Wilson, for Harrogate, conveyed that its residents would prefer the town to be sited at a greater distance from the city than the present fifteen miles. Sir Hubert Houldsworth, for Leeds, examined with forensic finesse Harrogate's title to any place on the map.

### Ciba Foundation

Sir George Lloyd-Jacob, one of Her Majesty's judges of the High Court of Justice, has been appointed a trustee of this Foundation.

### Army Appointment

Mr. R. J. V. Battle has been appointed honorary consultant in plastic surgery to the Army at Home in succession to Prof. T. Pomfret Kilner, who has retired on reaching the age-limit.

### London Medical Exhibition

The annual regional exhibition is to be held next year from May 7 to 11, at the City Hall, Cardiff. Further particulars may be had from the organisers of the London Medical Exhibition, 194, Bishopsgate, E.C.2.

### National Blood Transfusion Service

In the first six months of this year there were 379,282 donations of blood to the service. This is the highest total ever reached. Last year, in the same period, there were 344,269 donations. 59,551 people gave their blood for the first time in the same period, and at the end of June the donors' panel stood at 571,659, an increase in six months of over 31,000. The service still needs more regular donors to ensure that no-one need be asked to give blood more than twice a year, to replace the older donors when they reach 65, and to provide adequate reserves of blood-plasma.

### Anglo-French Exchange Bursaries

Applications are invited for bursaries to be awarded in 1956 to young British doctors under the exchange scheme arranged by the French Embassy in London between the Institut National d'Hygiène in Paris and the Ciba Foundation in London.

The value of the French grants is 60,000 francs a month, tax-free, and they will be awarded for periods of two to four months to doctors who wish to obtain clinical experience or carry out research in France. Since the aim of the exchange is to spread in each country knowledge of achievements, outlook, and methods in the other, preference will normally go to candidates who are in teaching, or in posts where they can pass on the experience they have acquired. Application forms may be had from Dr. G. E. W. Wolstenholme, Ciba Foundation, 41, Portland Place, London, W.1. The closing date for applications is Feb. 4, 1956.

---

The Association of Universities of the British Commonwealth (36, Gordon Square, London, W.C.1) has published the eighth edition of its annual list of awards tenable in the United Kingdom and of awards tenable overseas by United Kingdom graduates.

---

CORRIGENDUM: *The late Mr. A. R. Thompson.*—Mr. Thompson was assistant surgeon to the Victoria Hospital for Children in Chelsea, and not in Leeds as stated in our obituary (Nov. 19, 1955, p. 1092).

## Diary of the Week

DEC. 4 TO 10

### Monday, 5th

POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road, W.12
4 P.M. Dr. Raymond Daley: Aortic Stenosis.

LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE, Keppel Street, W.C.1
5.15 P.M. Miss Muriel Robertson, F.R.S.: Some Aspects of Trypanosomiasis, with special reference to the work of Sir David Bruce. (Manson lecture.)

NUTRITION SOCIETY
5 P.M. (1, Wimpole Street, W.1.) Dr. H. J. Deuel, jun. (Los Angeles): Fat as an Essential Component of Diet.

INSTITUTE OF CARDIOLOGY. National Heart Hospital, Westmoreland Street, W.1
9.30 A.M. Sir John Parkinson: Heart Attacks.

INSTITUTE OF CHILD HEALTH, The Hospital for Sick Children, Great Ormond Street, W.C.1
5 P.M. Prof. C. C. de Silva (Ceylon): Undernutrition and Kwashiorkor in Ceylon.

### Tuesday, 6th

ROYAL COLLEGE OF PHYSICIANS OF LONDON, Pall Mall East
5 P.M. Dr. C. E. Newman: External Reform and the Medical Act. (FitzPatrick lecture.)

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1
5 P.M. *Epidemiology and Preventive Medicine.* Dr. Alexander Langmuir (Washington, D.C.): Surveillance of Poliomyelitis in the U.S.A. in 1955.

BRITISH POSTGRADUATE MEDICAL FEDERATION
5 P.M. (London School of Hygiene and Tropical Medicine.) Prof. D. A. Slome: Physiology of Nasal Circulation.

KING'S COLLEGE HOSPITAL MEDICAL SCHOOL, Denmark Hill, S.E.5
4.30 P.M. Sir Russell Brock: Cardiac Surgery. (Thomas Percy Legg lecture.)

ST. MARY'S HOSPITAL MEDICAL SCHOOL, Paddington, W.2
5 P.M. Mr. Douglas MacLeod: Endometriosis.

INSTITUTE OF OBSTETRICS AND GYNÆCOLOGY
12 NOON. (Queen Charlotte's Hospital, Goldhawk Road, W.6.) Mr. H. R. MacLennan: Contracted Pelvis.

INSTITUTE OF NEUROLOGY, National Hospital, Queen Square, W.C.1
5.30 P.M. Mr. Harvey Jackson: Intractable Pain and its Surgical Treatment.

INSTITUTE OF DERMATOLOGY, Lisle Street, W.C.2
5.30 P.M. Dr. Brian Russell: Neurodermatitis.

CHELSEA CLINICAL SOCIETY
8.30 P.M. (Rembrandt Hotel, Thurloe Place, S.W.7.) Dr. Donald Teare, Sir Ronald Howe: Murder.

### Wednesday, 7th

ROYAL SOCIETY OF MEDICINE
5.15 P.M. *History of Medicine.* Dr. W. R. Bett: Trends in Medical Literature.

INSTITUTE OF OBSTETRICS AND GYNÆCOLOGY
3 P.M. (Hammersmith Hospital, Ducane Road, W.12.) Mr. Percy Malpas: Prolapse.

INSTITUTE OF DISEASES OF THE CHEST
5 P.M. (Brompton Hospital, S.W.3.) Sir Russell Brock: Surgery of the Aorta and Aortic Valve.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY
5.30 P.M. (Royal National Throat, Nose and Ear Hospital, Gray's Inn Road, W.C.1.) Prof. F. C. Ormerod: Surgery of Pharyngeal Carcinoma.

INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. R. W. Riddell: Moniliasis.

EUGENICS SOCIETY
5.30 P.M. (Royal Society, Burlington House, Piccadilly, W.1.) Prof. H. J. Eysenck, PH.D.: Nature and Inheritance of Extraversion.

MANCHESTER MEDICAL SOCIETY
4.30 P.M. (Medical School, University of Manchester.) *Medicine.* Dr. M. J. Greenberg: Diagnostic Problems in the Thorax.

ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW, 243, St. Vincent Street, Glasgow
5 P.M. Mr. L. N. Pyrah: Hormones in the Treatment of Cancer, with special reference to the Adrenal Gland. (Weild lecture.)

MEDICO-CHIRURGICAL SOCIETY OF EDINBURGH
8.30 P.M. (18, Nicolson Street, Edinburgh.) Dr. W. M. C. Harrowes: Place of Psychiatry in American Medicine.

### Thursday, 8th

ROYAL COLLEGE OF PHYSICIANS OF LONDON
5 P.M. Dr. Newman: Triumph of the General Practitioner and the Advent of Laboratory Medicine. (FitzPatrick lecture.)

BRITISH POSTGRADUATE MEDICAL FEDERATION
5.30 P.M. (London School of Hygiene and Tropical Medicine.) Dr. Audrey Smith: Experimental Hypothermia in Animals.

ROYAL SOCIETY OF MEDICINE
5 P.M. *Ophthalmology.* Mr. F. A. Williamson-Noble, Mr. E. J. Crundall, Mr. J. Pike: Multifocal Lenses.

INSTITUTE OF OBSTETRICS AND GYNÆCOLOGY
4.30 P.M. (Chelsea Hospital for Women, Dovehouse Street, S.W.3.) Mr. R. A. Brews: Vesicular Mole and Chorion Epithelioma.

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE, 26, Portland Place, W.1
7.30 P.M. Dr. P. H. Abbott: Mycetoma in the Sudan.

ALFRED ADLER MEDICAL SOCIETY
8 P.M. (11, Chandos Street, W.1.) Dr. E. K. Ledermann: Principles of Adlerian Psychology.

CHADWICK LECTURE
5 P.M. (Wright-Fleming Institute, Norfolk Place, Paddington, W.2.) Dr. R. M. B. MacKenna: Industrial Dermatitis. (Malcolm Morris lecture.)

UNIVERSITY OF ST. ANDREWS, Small's Wynd, Dundee
5 P.M. Dr. Kenneth Cowan: The Changing Scene.

### Friday, 9th

POSTGRADUATE MEDICAL SCHOOL OF LONDON
2 P.M. Prof. C. Gray: Jaundice.
4 P.M. Prof. A. W. Woodruff: Dysentery and its Management.

INSTITUTE OF OBSTETRICS AND GYNÆCOLOGY
2 P.M. (Queen Charlotte's Hospital, Goldhawk Road, W.6.) Prof. J. F. Cunningham: Abdominal Pregnancy.

ROYAL MEDICO-CHIRURGICAL SOCIETY OF GLASGOW
8.30 P.M. (243, St. Vincent Street, Glasgow.) Dr. A. K. Boyle and Dr. D. B. Murray: Studies in Hypothermia.

ROYAL MEDICAL SOCIETY, 7, Melbourne Place, Edinburgh, 1
8 P.M. Mr. P. M. Barnes: Blood Transfusion—Past and Present.

## Appointments

BARNS, T. E. C., B.M. Oxfd, M.R.C.O.G.: senior obstetrician and gynæcologist, West Cumberland group of hospitals.

HENDRY, G. A., M.B., B.SC. Aberd., D.M.R.T.: consultant radiotherapist, Newcastle regional cancer service.

MOORHOUSE, DOREEN, M.B. Leeds: registrar, The National Hospital, Queen Square, London.

TURNEY, J. P., M.B. Lond., F.R.C.S.: senior casualty officer, South East Northumberland H.M.C.

## Births, Marriages, and Deaths

### BIRTHS

BROADHEAD.—On Nov. 11 at Ryde Nursing Home, Isle of Wight, to Jill, wife of Dr. H. H. Broadhead—a daughter.

# "DISPLACEMENT" BEHAVIOUR AND "PSYCHOSOMATIC" DISORDER

S. A. BARNETT
M.A. Oxfd
LECTURER IN ZOOLOGY, GLASGOW UNIVERSITY

THE object of this paper is to suggest a relationship between the "displacement behaviour" described by ethologists,* and what clinicians sometimes call "psychosomatic disorder." The argument leads to two general sets of proposals. The first concerns the necessity for a particular line of research; the second suggests that the present terminologies of psychologists and psychiatrists are often a handicap on progress, and in particular that their interpretations should be strictly monist.

## Displacement Behaviour

Displacement behaviour is the performance of a behaviour pattern, in biologically inappropriate circumstances, when an appropriate action is prevented or the input to the central nervous system departs from the optimum. The behaviour does not directly serve the survival or reproduction of the individual or the species: biologically, it is irrelevant to the situation in which it is performed. Such behaviour has been mainly studied in fishes and birds (cf. Armstrong 1950, Tinbergen 1952), but it certainly occurs also in mammals. For example, a wild rat feeding, disturbed by another rat of a different species, makes "aggressive" noises and motions towards the interloper; the latter flees; the first rat then, instead of immediately resuming feeding, briefly grooms its face with its forepaws—an action which it would not ordinarily perform in the middle of feeding (Barnett and Spencer 1951). Deprived of the object of its aggression, the rat resorts to an alternative, and inappropriate, behaviour pattern. A slightly different example is that of wild rats during a series of copulations: at intervals both male and female may make a rapid move to a feeding-point, feed hurriedly (and in a quite atypical manner) for a few seconds, and then resume the usual pattern of courtship and coitus (unpublished).

In general, typical displacement activities occur in three types of situation. First, if an animal is interrupted in, or prevented from performing, a specific act, it may substitute another act, as in the example above of the aggressive rat. Second, seemingly irrelevant behaviour may occur if an animal has two incompatible types of behaviour open to it, as with herring gulls which resort to grass-pulling when the "appropriate" behaviour could be either to attack or to run away (Tinbergen 1953). Third, the actual attainment of a goal—the performance of a consummatory act—may, strangely enough, be followed by irrelevant behaviour, as in the example above of the rats between copulations.

Displacement activities are often incomplete actions, as in the nest-building movements of gulls or the grooming of rats; but they need not be so. They are often hurried, as in the displacement feeding of rats. The so-called vacuum activities, in which an animal performs an action, such as a display, in the absence of an appropriate object, may possibly be responses to suboptimal stimuli; they are comparable to displacement acts. Like them, they seem to reflect an "overflow" of motor output. This point will be discussed in more detail later.

Another phenomenon closely similar to displacement is the "redirection activity" (Bastock et al. 1953), in which an animal directs the appropriate movement towards an inappropriate object. The authors quoted refer only to examples where the appropriate object is still present; but a similar effect has been observed when the object is no longer available: a rat deprived of the object of its aggression may turn on a member of its own colony (Barnett and Spencer 1951). Bastock and her colleagues draw attention to the analogy to the "object displacement" of psycho-analysts. As Freud (1949) wrote:

> We have found that instincts can change their aim (by displacement) and also that they can replace one another—the energy of one instinct passing over to another.

The examples of displacement behaviour given above may be unconvincing to the critical reader who has not himself observed such behaviour. A critical attitude is very necessary in this field; but fortunately, as we shall see below, good examples, quantitatively analysed, do exist.

## Learnt Responses Resembling Displacement Behaviour

In the classical examples of displacement activity, the substituted behaviour always belongs to an alternative stereotyped ("innate") behaviour pattern. This is reflected in the first definition of the term "displacement activity" given by Thorpe (1951): such activity is said to "result from the activation . . . of the action pattern belonging to another instinct"; but alternative, wider definitions are given.

For the present argument it is convenient to apply a wider definition, such as that given at the beginning of this paper. We can then consider whether there are learnt responses in mammals which, though very different from displacement responses of the usual sort, can properly be put under this general heading. Maier (1949) describes experiments in which albino rats were faced with an insoluble problem in a Lashley jumping apparatus. Whatever solution they chose, they were "punished" in half of their jumps on the average. Moreover, they were forced to jump. Such rats tended to develop "behaviour-fixations": they commonly, after some time, jumped, say, always to the right, regardless of the stimulus situation; indeed, they did so even if the door was open and the food was visible on the left-hand side. Maier comments:

> It appears that the fixated group develops some kind of adjustment to the test situation and is therefore able to prevent emotional tensions.

Fixated rats also showed less resistance to making a jump. The detailed interpretation of Maier's results remains difficult and to some extent controversial, but there is no doubt, from his and other experiments, of the reality of "behaviour fixations" (Russell and Pretty 1951).

Better-known examples of "abnormal" learnt responses are those described under the heading of "experimental neurosis." In these, too, an insoluble problem may be presented, but the result is either an excessive undirected activity, or a general *in*activity which may include refusal of food. The variety of these "abnormal" acts is considerable (cf. Russell 1950), and a fuller analysis is needed before the validity of the comparison suggested here can be assessed. However, despite the diversity of these responses, there seems to be at least an analogy to displacement behaviour in all these examples: certainly, where there is a fixated response this provides a regular pattern of motor output in frustrating circumstances—i.e., in conditions in which a biologically appropriate response cannot be made.

## The "Consummatory Situation"

Usually, a displacement activity has been described as a substitute for an alternative *activity*: if an animal is unable to perform or to complete a consummatory act, such as fighting, feeding, or copulation, it performs

* Ethology is the scientific study of animal behaviour.

some other act instead. But this does not always apply. Moynihan (1953) studied nest-building movements and preening movements in gulls during incubation of the eggs. Nest-building movements were shown to increase if one or more eggs were removed, and the number of such movements in a given time increased in proportion to the number of eggs removed. Preening increased markedly only when all the eggs were removed. An important feature of this work was the quantitative expression of displacement behaviour: in this case, unlike many, subjective impressions could be excluded. (An earlier good example is that given by Tinbergen and van Iersel (1947) on fanning in *Gasterosteus aculeatus*.) Both types of movement were typical of displacement activities, in that they belong to stereotyped behaviour patterns, and that they occurred at inappropriate moments. They differed from the usual examples, however, in one notable respect: they were performed, not in place of a motor act, but when a specific sensory situation was altered. The substitute activity reflected the absence of what might be called a "consummatory situation" (cf. Thorpe 1954).

The importance of the afferent input is also shown by the work of H. Spurway and J. B. S. Haldane on the air-gulping of the climbing perch (*Anabas testudineus*). Haldane (*in litt.*) writes:

> Our fish got into a flap when they breathed $N_2$. To men this certainly has not got an odd smell or taste. It makes you feel dizzy a few seconds after breathing it. Probably the brain is also affected by afferent impulses from the carotid sinus. The fish have done their consummatory act, but have not got the normal "feedback." This disturbs them much more than if they are mechanically prevented from carrying out the act.

It seems reasonable to suggest that the concept of consummatory situation or state is more fundamental and more general than that of consummatory act. The latter marks the end of activity, or at least of a specific group of activities, such as those related to mating. But the performance of such an act must be accompanied by specific internal changes, such as those involved in filling the stomach; and these changes, by evoking a particular afferent input, thereby alter central nervous activity and so the output to the muscles.

### "Instinct" in Man

Kennedy (1954), in a polemical discussion of ethological theories, suggests that the cessation of activity on the attainment of a consummatory act is "reflex"—i.e., due to an input of impulses from the periphery. Bastock et al. (1953), in the paper already quoted, suggest that "consummatory stimuli," and especially proprioceptive feed-back, are important in what they call the "consumption of drive." (Since proprioceptive fibres make up one-third to one-half of those in a nerve supplying a muscle, it is clear that they deserve a good deal of attention in the study of behaviour (cf. Lissman 1950).) Disregarding the particular terminologies used in these two communications, each, from different points of view, suggests that we must look to the afferent input if we are to make a beginning on the physiological analysis of displacement behaviour.

It is therefore worth while to consider a little further the subject of the influence of afferent impulses on certain sorts of behaviour. Here is an example (Hardy 1954) from a physiological study in which engineering and psychiatric terms are both used in a physiological context:

> From the point of view of servo control of skin temperature, it is worth noting that thermal sensations have strong elements of unpleasantness or pleasantness when the average skin temperature is below 32° or above 34°C . . . .This "affect" of thermal sensation is probably one of the most powerful drives for physiologic servo temperature regulation in the presence of external thermal stress.

A noxious stimulus of the sort described here evokes in man either a general restlessness (analogous to appetitive behaviour), or a learnt response which tends to reduce the unpleasantness. If there is no learnt response available, as in a young child, the restlessness may lead to learning—perhaps of the trial-and-error variety. In any case, the situation described in the quotation above is one in which a particular sensory condition induces activity, and this activity ceases on the attainment of a "consummatory situation"—in the example, a particular skin-temperature.

If the analysis above is correct, it may serve to clarify the concept of "instinct" as applied to man. In ethological writing the term "instinct" is today commonly (not always) applied to a stereotyped *activity*. Depending on the author, the activity may be a single consummatory one; or it may be a complex series of acts, of which the consummatory one is the last. The term instinct, *so used*, does *not* apply to any internal agency in behaviour, though the term "drive" may be used to refer to internal influences which lead to the activity.

In man there is virtually no instinctive behaviour in the above sense. The infant breathes, sucks, and cries; he also, perhaps, at 3–6 months, smiles in response to a particular "sign stimulus" (Spitz and Wolf 1946); but apart from reflexes, later behavioural performances are learnt. Yet human beings act most strenuously to achieve certain ends. These ends, regarded at the physiological level, are the attainment of certain sorts of neural input—of consummatory situations. The motor procedures which attain these ends are variable and learnt.

Hence, to take an example from Freud, the word *Trieb*, usually translated as "instinct," refers to behaviour which ceases once a particular nervous input—e.g., from a full belly or empty seminal vesicles—has been achieved. Or, to put the obverse, the behaviour is activated by the input from an empty belly or full seminal vesicles. These examples must not be taken to imply that all such behaviour is activated peripherally, by the stimuli of the moment, or that it is "innate." In "higher" mammals, especially man, with a vast mass of internuncial neurons in the cerebral cortex, it seems that learning—or at least previous experience—may lead to forms of neural organisation in which the activation of the motor output is largely within the central nervous system itself. Behaviour may then be both "spontaneous" and a product of learning.

As Hebb (1949) has pointed out, it is this internuncial mass which makes possible the predominance of learnt behaviour in man, and his relative independence of the immediate sensory situation. Whitehorn (1952) approaching this topic from the point of view of a psychiatrist, has remarked that, despite the evidence from social anthropology for the cultural rather than the innate patterning of human behaviour, the term instinct is still retained by psychiatrists. He points out that the psychiatric use of the term represents a shift of meaning [from that of ethologists] to "inner driving forces correlated with biological needs," and that "this inner impulsive force is experienced as emotion." He further suggests that "emotion" is negatively correlated with instinctive behaviour: the less an animal's behaviour is automatically determined by fixed neural patterns, the more it is necessary that powerful internal agencies should ensure that effective behaviour patterns are acquired (learnt) by each individual. Emotion in this context is the subjective counterpart of the neural changes due to a certain type of (unpleasant) sensory input.

Whether or not we agree with this hypothesis about "emotion," Whitehorn's analysis brings out clearly the notorious fact that the term "instinct" is what Ogden and Richards (1931) call a nomad: it wanders

from meaning to meaning. It is to be feared that its wanderings are not yet over.

## "Psychoneurosis" and "Psychosomatic" Disorder

*Behavioural Changes*

In the virtual absence of instinctive behaviour in man, one might think it idle to look for displacement activities in human behaviour. The realisation of the importance of "consummatory state," however, alters the picture.

The analogy between displacement behaviour in other animals, and psychoneurotic behaviour in man, has indeed often been pointed out, notably by Armstrong (1950). Armstrong quotes a passage on hysteria in which Freud writes that in such states "we have an excessive innervation (in typical cases a somatic innervation), sometimes of a sensory, sometimes of a motor character, either as an excitation or an inhibition." This refers of course to the fact that the behaviour called hysterical covers a wide range, from outbursts of weeping to a functional paralysis or anæsthesia. Armstrong comments that both in displacement behaviour and conversion hysteria "the performance . . . is a somatic means of release from tension; in both the activity is incomplete and apparently detached from normal affective experience." The same might be said of obsessional behaviour. However, the fact that hysteria includes phenomena of inhibition, as well as overt activity, must make one hesitate to regard it, in any simple way, as the human counterpart of displacement behaviour. As we shall see, this sort of question can be answered, or indeed effectively asked, only in neurophysiological terms.

Psychoneurotic behaviour in general is of course not "instinctive": it does not consist of rigidly stereotyped activities common to a whole species or variety; in a sense it is learnt. Behaviour, such as smoking or chewing, which is clearly analogous to displacement behaviour but which perhaps ought not to be labelled psychoneurotic, is quite obviously learnt. The same applies to the thumb-sucking of an infant. (Smoking and the rest could be labelled "abnormal," whatever that may mean, but there are other human responses, of biological value and in no possible sense pathological, which may have originated, in evolution, as displacement behaviour. Spurway and Haldane (1953) suggest that speech is a derivative ("ritualised") of displacement breathing. Another form of communication, the movements of the facial muscles of expression, may well have originated in the same way, and have acquired increasing importance with the development of human society.)

At this point a warning is perhaps required. It is obvious, but sometimes overlooked, that human behaviour is so much more complex than that of any other species, that it is in some respects qualitatively as well as quantitatively different. This is evident in our use of symbols, not only in language but also indirectly. If a woman is "sick of" her husband, she may not say so or give any verbal indication that she is aware of it: but she may persistently vomit while her husband is at home. (I am indebted to Dr. R. D. Laing for this example.) Such a response can be interpreted according to a variety of systems. It could be described in neurological terms, perhaps with the addition of expressions derived from studies of conditioned reflexes; it could be compared to a displacement response; or it could be characterised in the more poetic or symbolic phrases (no sneer is intended) of Freudian analysis. All no doubt have some validity, but to say that psychoneurosis resembles displacement behaviour certainly does not "explain" it.

The usefulness, if any, of the sort of comparison made here is of two kinds. First, if similar processes are found in man and other species, research possibilities may be widened. The proposal is then, in effect, a hypothesis, namely, that similar internal "mechanisms" underlie all the various phenomena compared. Secondly, the attitude to particular aspects of human behaviour may be changed for the better. The objective, non-ethical, approach to behaviour attempted by ethologists is superior to a subjective moralistic one, both heuristically and humanely. Yet if a person is said to have a "mental" disorder, for many—even for some doctors—this amounts to a moral stigma or æsthetic flaw, such as is not felt to exist in the person with, say, peptic ulcer or tuberculosis. (It is perhaps instructive to realise that a great variety of so-called "perversions," from masturbation to fetishism, have been observed in various animal species. Homosexuality, in particular, is a widespread phenomenon among vertebrates.) There is, indeed, on these grounds alone, a case for revising the terminology of what, in my view, should be called behaviour disorders but which at present are usually described as mental illnesses. (It is a strange fact that in psychiatry the term "behaviour disorder" is reserved for a single group of antisocial activities—the "conduct" disorders which are also lumped under the head of "psychopathic personality.")

*Somatic Responses*

In all the examples so far given, there is an altered output from the central nervous system. Instead of the biologically appropriate or "normal" output, another is substituted. The alternative motor pattern may be "instinctive" or not; it may be alternative to an active pattern of behaviour or to an inactivity; it may itself be an inactivity—an inhibitory effect.

All these statements apply also to the so-called psychosomatic disorders of man. In these, the substitute output is not to the somatic musculature, but is as a rule autonomic. There is, however, no part of the body and no organ which is outside the scope of these disorders. This is not surprising, since every part of the body has a blood-supply partly under autonomic control and carrying hormones of which the secretion is influenced by the autonomic nervous system.

Wolff (1953) gives an excellent review of these conditions. An example is the pattern of response of the stomach to the ingestion of food: increased blood-flow, increased motility, and secretion of acid. These may all occur, quite inappropriately, in conditions of stress. Another familiar response to stress is diarrhœa—hyperactivity of the gut muscles. Wolff comments that the person with violent diarrhœa may be outwardly "calm, sweet-mannered and serene." A third standard example is asthma, in which the response is an inappropriate contraction of the smooth muscle of the lung.

Alexander (1952a) describes these responses as follows:

> Whenever the expression of competitive, aggressive, and hostile attitudes is inhibited in voluntary behaviour, the sympathetic adrenal system is in sustained excitation. The vegetative symptoms result from the sustained sympathetic excitation, which persists because no consummation of the fight or flight reaction takes place in the field of co-ordinated voluntary behaviour, as exemplified by the patient suffering from essential hypertension who in his overt behaviour appears inhibited and under excessive control. Likewise in migraine headache, the painful attack may terminate within a few minutes after the patient becomes conscious of his rage and gives open expression to it.

It is easy to see that, in one aspect, the psychosomatic responses fit quite readily into a Pavlovian framework: they can be interpreted in terms of conditioned reflexes, once it is understood that a conditioned reflex is an exceedingly complex phenomenon (cf. Hebb 1949). In each instance the primary response is "innate," and would ordinarily be called reflex. In the innate character of the response, these disorders show a closer similarity to the ordinary displacement behaviour of

birds and fishes, than is shown by typical "psychoneurotic" behaviour. They are, however, different in three obvious ways from what we may call classical displacement activities.

First, they are very variable within the species. There is evidence, as might be expected, of genetically determined differences in the ways in which individuals react to stress: in one man a given stress may induce, say, diabetes, in another similar conditions may lead to hypertension. This is perhaps yet another example of the exceptional polymorphism of the human species (cf. Haldane 1949).

Second, the environmental causes of these disorders is much more complex and diffuse. Even when there is an immediate precipitating cause, it acts on a central nervous system already prepared by previous experience. This of course reflects the size and complexity of the human nervous system, with its enormous accumulation of connecting neurons.

Third, as already mentioned, the output is not somatic motor, but is visceral. Here again, evidently, we have a reflection of a distinctively Primate (especially human) evolutionary development—namely, the importance of the cerebral cortex, and especially of the frontal lobe, in controlling autonomic output. Fulton (1949) writes:

> I am inclined to regard the recognition of the frontal lobe as the primary autonomic centre of the forebrain as perhaps the most significant disclosure of recent years in the field of scientific medicine, for it affords at long last a sound physiological background for that still shadowy subject of "psychosomatic medicine."

Despite these differences, the psychosomatic disorders and the psychoneuroses on the one hand, and displacement activities on the other, all seem to exemplify a general feature of complex nervous systems—that, if there is an excitatory state which would ordinarily produce a motor discharge, and if the motor output cannot take place in the biologically "normal" fashion, then it will follow some other path. The other path may be "innate" or "learnt," but, if learnt, may be rigorously fixed for the particular individual.

## The Problem of "Nervous Energy"

*Terminology*

An early discussion of "nervous energy" was that of Freud. As Ernest Jones (1953) points out, Freud in his early psychiatric works wrote in terms of "an economics of nervous energy." (At that time, too, Freud adopted a notably "psychosomatic" approach to his subject. In interpreting anxiety neurosis as a consequence of sexual deprivation he points out that increased respiration-rate, palpitation, sweating, and congestion occur both in coitus and in anxiety states. As Jones shows, the history of Freud's thinking is of great interest for the study of ideas on the relation between "soma" and "psyche.")

What, then, is the nature of the central state responsible for the motor discharge? This is as crucial a question for ethology as for psychology. Whether the central state is in turn due to a specific neural input, or whether it is in any sense autonomous, there can be no doubt that it exists. Lorenz (1950) interpreted the variation in intensity of "innate behaviour patterns" in terms of "reaction specific energy." This expression has been extensively criticised, and Thorpe (1951) proposed the use of the term "specific action potential" (S.A.P.), later modified to "specific action potentiality," as an alternative. The definition is:

> "The state of the animal responsible for its readiness to perform the behaviour patterns of one instinct in preference to all other behaviour patterns. This specific readiness diminishes or disappears when the consummatory act of the discharged instinct has been performed."

The advantage of this term, so defined, is that it is objective, unambiguous (provided that terms such as "instinct" are defined with similar rigour), and non-committal on the nature of the internal state involved. The last feature might however be regarded as a disadvantage, since it glosses over the major problem—namely, the nature of the central state of "readiness."

Whatever terminology is adopted, if the suggested relationship between displacement behaviour and certain human disorders has any significance, it should lead to some improvement in our understanding of behaviour. I suggest that it can do this in two ways.

*Possibilities for Research*

Halstead (1951) has remarked that a major gap in neurophysiology is our ignorance of how the output of the cerebral cortex is organised. For mammals it is of course just this output which is crucial for understanding the behaviour discussed here. The need for links between neurophysiology and ethology has been urged often enough (cf. Darwin 1872, Tinbergen 1951), but the links are slow in the forging. We have seen that there is a general rule that, if one motor output is blocked, for whatever reason, there will be discharge along another pathway. Can physiologists make this notion more precise, in terms of the actual functioning of neurons? One of the great difficulties is to decide on a line of attack. What experiments can be devised to establish specific relationships between neural processes and behaviour? Up to now, there has been more success in relating hormonal effects to specific behaviour patterns, but we know almost nothing of how the hormones influence the central nervous system—or, for that matter, how the nervous system influences endocrine secretion.

Nevertheless, it seems possible that this is a field in which advances might soon take place, given sufficient effort. The phenomena of "stress" (cf. Selye 1950) have already been mentioned in connection with psychosomatic responses. They have been studied especially in man and laboratory mammals, in which they involve a complex tangle of relationships between the endocrine glands, the hypothalamus, and the cerebral cortex. Selye has described a "general adaptation syndrome," involving a characteristic set of changes in endocrine and other organs, and leading sometimes to "psychosomatic" disorder. Despite controversy on detail, we have the beginning of a foundation for the physiological study of these disorders (cf. Russell 1953).

Parallel studies come from the psychological side, apparently uninfluenced by developments in ethology, but with a bearing on them. Stellar (1954) has put forward a hypothesis that "motivated behaviour" is quantitatively dependent on the activation of hypothalamic centres. He uses Morgan's term "central motive state" as his counterpart of the ethologists' S.A.P. He suggests that, if the hypothalamus is indeed concerned in the control of all types of "motivation," this may help to account for "interaction among motivations." Brain function is likely to be more complex than this suggests (cf. Fessard 1954), but in so far as it is valid, it has obvious implications for the understanding of displacement behaviour in vertebrates. Psychologists have also carried out experimental work with results which ought to be incorporated in any general picture. Maier's work has already been mentioned. Miller (1948) has shown that white rats may show "generalisation (of response), or displacement . . . from one drive to another."

The physiological side has been emphasised here, because it seems essential, for real progress, that a physiological analysis of behaviour should be developed. But this does not imply that the study of overt behaviour should be neglected. There is also needed, among much else, a thorough study of the whole range of substitute responses throughout the vertebrates at least: such a survey should preferably be carried out in conjunction with physiological studies.

*Language and Interpretation*

In this endeavour, it will be necessary to join the efforts of people working in widely different fields. The gulfs between psychiatry, psychology, ethology, and physiology are both wide and deep, and the attempt to bridge them is liable to bring on fits of dizziness. An urgent necessity is for those who practise one discipline to learn the language of the others. It would perhaps be naïve to hope for a unified terminology, at least in the next few decades, but some simplification might be attempted. Psychiatrists often use words in ways which bewilder outsiders and perhaps repel students. Here, for instance, are two statements by an authoritative follower of Freud—Franz Alexander (1952b):

> In early infancy the uncoördinated movements of the child are not yet subordinated to any utilitarian goal and probably have the sole function of erotic discharge.
>
> Erotic phenomena have a playful quality—in fact, all play activities are erotic in nature.

Such statements may have a valid meaning; but to a biologist they suggest a lack of rigour in the use of language: what does "erotic" mean in these sentences?

It is not suggested that clinicians will derive much *direct* benefit, as clinicians, from watching rats or seagulls, or from reading about them. But some intellectual stimulation may result, and perhaps a more critical approach to theory and a more rigorous terminology. In particular, one fundamental conclusion arises from the argument presented here—that a monistic frame of reference is the only one which satisfies the needs of communication about behaviour. We are obliged to speak of the animal body, including that of man, as a material entity, of which the existence can be fully explained in terms of the observable, physical processes going on in it. This excludes any reference to a "mind" in the sense of an independent agency or separate mode of existence (cf. Young 1950).

This statement is not intended as an excursion into theology, or even epistemology. Nor does it deny the reality of consciousness. Our consciousness is tied firmly to the integrity of certain parts of our brain: we are conscious when certain neural processes are occurring, and unconscious when they are not. When we say, colloquially, that we have something "in mind," we refer to our conscious thoughts; but there is no reason why we should reject the notion that these thoughts are reflections, or aspects, of brain function.

It is assumed that the aim of ethology, of which psychology is a part, is the fullest possible understanding and consequently prediction and control, of behaviour. To improve understanding, we have to devise ways of communicating our observations and theories about behaviour. At present, however, dualistic modes of speaking are so deeply embedded in our language, that a man may explicity support monism, and in the same breath use a dualistic terminology. The obvious example is the persistence of the division of illness into "mental" and "physical."

We can see this very clearly with the "psychoneuroses" and the "psychosomatic disorders." As their names imply, the mind or psyche is held to be involved in both: the first, however, are commonly regarded as strictly "mental" disorders, while the second are, by definition, diseases in which the manifestation is "somatic." The distinction, however, disappears when we find that the two kinds of condition may alternate or co-exist in the same individual: a man with persistent pulmonary tuberculosis, given a phrenic crush which improves the condition of the lung, develops a conversion hysteria instead (Day 1946); similarly, anxiety may be without any manifestation in talk or other behaviour when there are "somatic" indications of stress, although the somatic state disappears when anxiety is removed.

From this point of view the common practice of using the term "neurosis," instead of "*psycho*neurosis," is appropriate; but "neurosis" should include, not only conditions such as anxiety states or obsessional behaviour, but also "adaptive bodily changes with repression or denial of anxiety and other disturbances in feeling, with no verbalisation of conflicts except after considerable enquiry" (Wolff 1953); in other words, it should include the psychosomatic disorders, and all these disorders might more reasonably be called "neurogenic." The term "somato-somatic" has been suggested, not very seriously, for this approach (Schorstein 1954). Russian physiologists use the term "cortico-visceral" to refer to the effects of emotion on smooth muscle or glandular secretion.

(It would be wrong, no doubt, to pursue etymology much further. But it is remarkable that the terms "anxiety" and "angina" both have the same origin, which they share with the Latin verb *angere*, to choke. There are other instances of monism in etymology.)

A difficulty in the approach suggested here is that one can palpate a spastic colon, while the neural changes of an anxiety state can be inferred only from general behaviour or from speech. A psychologist or physician, accustomed either to the somatic or the "psychic" frame of reference, finds difficulty in switching to the other. This example further underlines the desirability of psychiatrists, psychologists, and ethologists learning each other's languages. Another, related, difficulty is that the way of speaking adopted here is, to some people, distasteful or even odious: to them it seems inhuman. This attitude deserves respect, since it often reflects a real and necessary concern with the needs of the whole human personality. The question remains, however, whether the formulations suggested in this paper help towards the successful application of knowledge to human ends. The ends to which knowledge is put depend on the motivation of scientists, physicians, and others, not on their prose style.

It is not suggested for a moment that only doctors use imprecise or obscurantist terminologies. The example of "instinct" has already been mentioned. "Drive" remains an instance of a mendicant word—one which goes around begging for a meaning (Ogden and Richards 1931). The whole of learning terminology, despite the efforts of Thorpe (1950) and others, is in a most unsatisfactory state (cf. Haldane 1954).

This state of affairs will not be remedied by logical meditation or semantic analysis alone. Greater precision must depend on improved understanding, and this will develop only from further experiment. The proposals put forward here for future research and for more rigorous interpretation are therefore interdependent.

## Summary and Conclusions

Disturbed behaviour, in which one reaction pattern replaces another, more "appropriate" one, is widespread in vertebrates. It occurs when an activity is interrupted or prevented (i.e., in "conflict" or in "frustrating" circumstances) or when a particular sensory situation is not achieved (e.g., when the number of eggs in a nest is reduced, or when the skin-temperature is outside a certain, optimum, range).

In the study of animal behaviour (ethology), responses of this sort are called displacement behaviour. These responses have been mainly described as substitutes for other *activities* (usually for consummatory acts such as breathing, eating, or copulating), but it is suggested that the immediate cause of such behaviour must always be some deficiency in the afferent input to the central nervous system. All activity is accompanied by a proprioceptive (and interoceptive) input, and this is presumably responsible for the normal cessation of

activity which occurs when a consummatory act has been performed.

In human behaviour there is an almost complete absence of "innate" behaviour in the sense of unlearnt stereotyped reaction patterns. Human behaviour of the kind which is said to arise from "instinct" is infinitely variable (apart from reflexes) on the motor side; but it tends to achieve particular sensory inputs (consummatory situations). If such ends are not attained, behaviour may be disturbed: "psychoneurotic" behaviour—e.g., in hysteria or obsessional states—is analogous in certain respects to displacement behaviour in birds or fishes. Psychoneurotic behaviour is, however, not innate, but in a sense learnt. In this it resembles the behaviour fixations developed by, for instance, rats in frustrating situations.

In these examples one motor output is substituted for another. The same applies in the "psychosomatic" disorders of man, in which an autonomic discharge, resulting from some form of "stress," produces a condition such as asthma. It is suggested that the distinction between psychoneurotic and psychosomatic disorder is unjustified; that both might properly be called "neurotic" or "neurogenic"; and that the distinction arises from a conventional mind-body dualism which is now a handicap in the interpretation of behaviour.

It is further suggested that displacement behaviour and neurotic responses of all kinds may represent a general feature of the functioning of nervous systems—namely, that if there is an excitatory state which would ordinarily produce a motor discharge, and if the motor output cannot take its "normal" form, then it will follow some other pattern. This proposal may be regarded as an hypothesis. It requires investigation and clarification by neurophysiologists.

In general, there is need for more effective communication between ethologists, psychologists, physiologists, and psychiatrists, and for the development of research in which physiologists and students of behaviour collaborate. Given such combination, it should be possible to devise experimental programmes which would lead to a rapid advance in the understanding of behaviour.

I am grateful to Prof. T. Ferguson Rodger and his colleagues of the Department of Psychological Medicine, Glasgow University, and to Prof. J. B. S. Haldane, F.R.S., and Dr. H. Spurway, for illuminating discussions on the subject-matter of this paper. Especial acknowledgment is due to Dr. A. B. Sclare for reading and criticising the manuscript.

### ADDENDUM

After this paper was written Kortlandt (1955) published a long and valuable discussion of the concept of instinct, with many references to the relationships between ethological and psychiatric theories. I have also been allowed to see, in advance of publication, a paper by Morris in which an interesting aspect of the connection between autonomic function and behaviour is presented. Both papers can be recommended to anyone interested in the topics I have discussed.

### REFERENCES

Alexander, F. (1952a) Psychosomatic Medicine.
— (1952b) *In* Alexander and Ross's Dynamic Psychiatry. Chicago.
Armstrong, E. A. (1950) *Symp. Soc. exp. Biol.* **4**, 361.
Barnett, S. A., Spencer, M.M. (1951) *Behaviour*, **3**, 229.
Bastock, M., Morris, D., Moynihan, M. (1953) *Ibid*, **6**, 66.
Darwin, C. (1872) The Expression of the Emotions in Man and Animals. London.
Day, G. (1946) *Lancet*, ii, 703.
Fessard, A. E. (1954) *In* Brain Mechanisms and Consciousness (edited by J. F. Delafresnaye). London.
Freud, S. (1949) An Outline of Psychoanalysis. London.
Fulton, J. F. (1949) Functional Localisation in the Frontal Lobes and Cerebellum. Oxford.
Haldane, J. B. S. (1949) *In* Genetics, Paleontology, and Evolution. Princeton and Oxford.
— (1954) *Behaviour*, **6**, 256.
Halstead, W. C. (1951) *In* Cerebral Mechanisms in Behaviour. New York.

*References continued at foot of next column*

# BIOPSY OF THE RECTUM IN ULCERATIVE COLITIS

GEORGE LUMB
M.D. Lond., M.R.C.P.
READER IN PATHOLOGY, WESTMINSTER MEDICAL SCHOOL
CONSULTANT PATHOLOGIST

R. H. B. PROTHEROE
B.A., M.B. Camb.
SENIOR REGISTRAR IN PATHOLOGY, AND RESEARCH FELLOW IN ULCERATIVE COLITIS

WESTMINSTER HOSPITAL, LONDON

RAPID autolysis has hitherto greatly impeded study of the morbid histology of the gastro-intestinal tract. For this reason post-mortem material is of very limited value for detailed study, and examination of surgical specimens also has its limitations because of the degenerative changes that occur before fixation is complete. The stomach and the rectum, however, are accessible for biopsy and the gastric mucosa has been carefully studied with the biopsy gastroscope. Palmer (1954) has used this method extensively and reviewed the published reports. Rectal biopsy has been used almost entirely for diagnosing

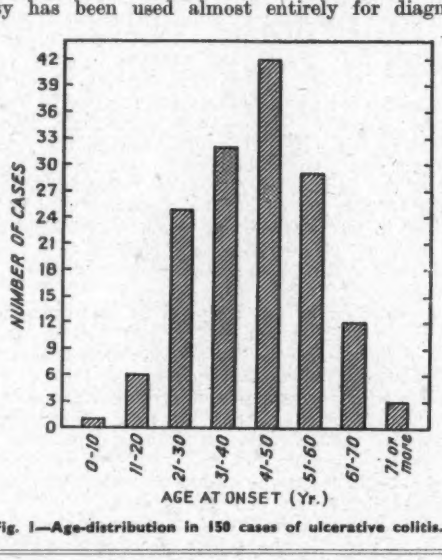



**Fig. 1—Age-distribution in 150 cases of ulcerative colitis.**

### MR. BARNETT: REFERENCES—*continued*

Hardy, J. D. (1954) *Harvey Lect.* **49**, 242.
Hebb, D. O. (1949) The Organization of Behaviour. New York.
Jones, E. (1953) Sigmund Freud, Life and Work. London; vol. i.
Kennedy, J. S. (1954) *Brit. J. anim. Behav.* **2**. 12.
Kortlandt, A. (1955) *Arch. Néerl. Zool.* **11**, 155.
Lissman, H. W. (1950) *Symp. Soc. exp. Biol.* **4**, 34.
Lorenz, K. Z. (1950) *Ibid*, p. 211.
Maier, N. R. F. (1949) *Frustration*. New York.
Miller, N. E. (1948) *J. abn. soc. Psychol.* **43**, 155.
Morris, D. *Behaviour* (in the press).
Moynihan, M. (1953) *Ibid*, **5**, 58.
Ogden, C. K., Richards, I. A. (1931) The Meaning of Meaning. London.
Russell, R. W. (1950) *Brit. J. Psychol.* **41**, 95.
— (1953) *Int. J. Psycho-Anal.* **34**, 1.
— Pretty, R. G. F. (1951) *Quart. J. exp. Psychol.* **3**, 151.
Schorstein, J. (1954) Personal communication.
Selye, H. (1950) The Physiology and Pathology of Exposure to Stress. Montreal.
Spitz, R. A., Wolf, K. M. (1946) *Genet. Psychol Monogr.* **34**, 57.
Spurway, H., Haldane, J. B. S. (1953) *Behaviour*, **6**, 8.
Stellar, E. (1954) *Psychol. Rev.* **61**, 5.
Thorpe, W. H. (1950) *Symp. Soc. exp. Biol.* **4**, 387.
— (1951) *Bull. anim. Behav.* **9**, 34.
— (1954) *Nature, Lond.* **174**, 101.
Tinbergen, N. (1951) The Study of Instinct. Oxford.
— (1952) *Quart. Rev. Biol.* **27**, 1.
— (1953) The Herring Gull's World. London.
— van Iersel, J. J. A. (1947) *Behaviour*, **1**, 56.
Whitehorn, J. C. (1952) *In* Alexander and Ross's Dynamic Psychiatry. Chicago.
Wolff, H. G. (1953) Stress and Disease. Springfield, Ill.
Young, J. Z. (1950) Doubt and Certainty in Science. Oxford.

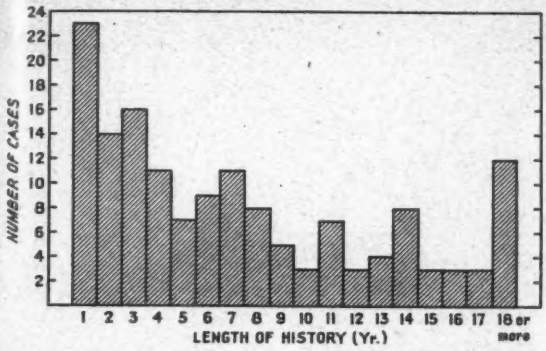



Fig. 2—Distribution of length of history in 150 cases of ulcerative colitis.

neoplasms (Gabriel et al. 1951), very little attention being paid to other mucosal abnormalities.

We describe here the histological changes seen in 180 biopsy specimens from the rectum in 150 cases of ulcerative colitis. The patients investigated were unselected, and material was obtained both in acute and in quiescent phases of ulcerative colitis. Figs. 1 and 2 show the age-distribution and the duration of symptoms in the series of ulcerative colitis.

### Technique

All the biopsy specimens were taken under direct vision with Officer's forceps through a sigmoidoscope. The level selected was 11 cm. from the anal sphincter because this is well above the anorectal junction yet below the peritoneal reflection. No anæsthetic was used, and except in 1 case in which there was slight bleeding, the patients suffered no discomfort and there was no adverse effect on the course of the ulcerative colitis.

Each specimen was bisected and placed in Susa fixative for twelve hours. Histological sections were cut 5 μ thick and stained routinely with Weigert's hæmatoxylin and azo-eosin. This method of fixation and staining gave the most precise results. Special stains for mucin fibrous tissue, and other substances were used as required.

To obtain an exact picture of normal rectal mucosa, 100 biopsies were done by the same technique on patients with hæmorrhoids or other conditions where sigmoidoscopy was required but the rectal mucosa was completely normal.

We also studied the healing of normal rectal mucosa after trauma. We asked our surgical colleagues to remove pieces of normal rectal mucosa when they were taking biopsy specimens from tumours of the rectum before surgical removal. These specimens were taken from two to twelve days before abdomino-perineal resection, so that various stages of repair could be studied.

### Normal Rectal Mucosa

The mucosa of the large intestine does not form folds, except in the rectum. Being devoid of villi it has a smooth surface. The crypts of Lieberkühn are straight tubules and in the rectum attain a length up to 0·7 mm. They are somewhat shorter in the colon. These glands are remarkably symmetrical in normal rectal mucosa and lie parallel and very close to each other (fig. 3). The free surface between the openings of the glands is lined by simple columnar epithelium with a thin striated border and by occasional goblet-cells. There are more goblet-cells at the top than at the bottom of the crypts. The other cells at the bottom, except an occasional argentaffin cell, are undifferentiated epithelial-cells often showing mitosis (fig. 4). Florey (1932) has shown that the goblet-cells are derived from undifferentiated epithelial-cells at the base of the crypts. Once a cell secretes mucus, it seems unlikely that it can revert to an undifferentiated cell although it may acquire a striated border.

The lamina propria in the healthy rectum is scanty. It contains a stroma of argyrophilic fibres similar to that of lymphatic tissue and becomes condensed to a reticular basement membrane at the epithelium-covered surface. Close to the fibres lie cells which have oval pale nuclei, may become macrophages, and can take up pigment. Among the meshes of this framework there is a moderate number of free cells, most of which are lymphocytes and plasma-cells with occasional eosinophils and polymorphonuclear leucocytes. Scattered lymphatic nodules, which reach their highest development in the rectal mucosa of man, are more numerous in the rectum than in the colon, and tend to increase progressively in number from the proximal to the distal large intestine (Dukes and Bussey

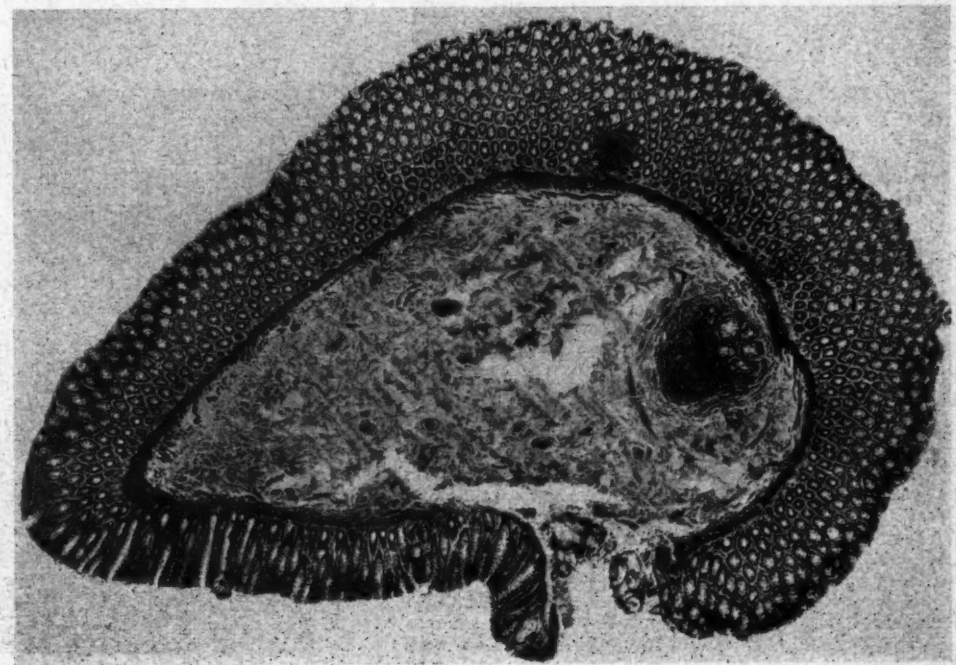


Fig. 3—Normal rectal biopsy specimen. (Hæmatoxylin and eosin. × 25.)

1926). They are of various sizes and often traverse the fibres of the muscularis mucosæ. The muscularis is well developed and consists of longitudinal and circular strands.

The submucosa does not present any peculiarities. It consists of thick collagenous and elastic fibres with small arterioles, venules, and lymphatics.

The biopsy specimens obtained from healthy rectum are remarkably similar. Since the biopsy forceps tend to remove part of a mucosal fold, the shape of the biopsy specimen is usually as seen in fig. 3. The 100 specimens examined include examples from both sexes and from all age-groups, and there is no evidence of any recognisable variation of appearance. Most of the crypts are seen cut transversely, and their closely packed and regimented arrangement with underlying sharply demarcated muscularis mucosæ is strikingly constant. In none of the normal biopsy specimens examined was there any evidence of infiltration by neutrophils or of degenerative changes in the epithelial-cells lining the crypts.

### Normal Process of Repair in Rectum

Mucosal repair has not been studied in the colon as extensively as in the stomach and small intestine. This is rather surprising because the structure of the mucosa is simpler in the colon than in the stomach and small intestine since it is not complicated by glands secreting digestive ferments.

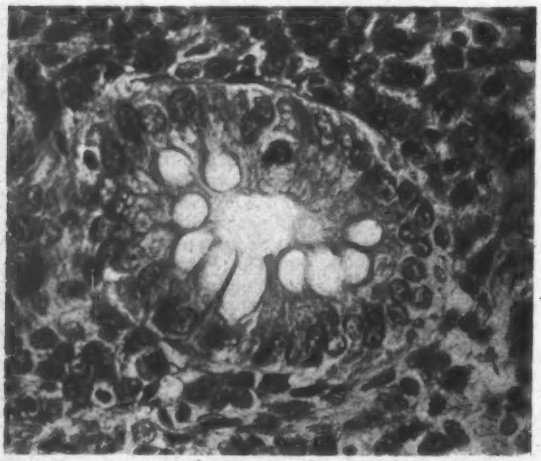


Fig. 4—Transverse section of base of normal crypt showing dividing cell. (Hæmatoxylin and eosin. × 576.)

Florey (1933), who was primarily interested in the rôle of mucus in protecting the colonic mucosa, found that, when the epithelium desquamated, the surviving cells tended to make good the deficiency by spreading laterally, first becoming cuboidal and finally becoming much flattened and in this way covering a considerable area of stroma. The many basophil dividing cells in the bases of the crypts of Lieberkühn are clearly the source of replacement of cells in the superficial portions of the glands and the intervening surface epithelium (fig. 4).

Localised areas of alimentary mucosa have been removed in animals, and the results vary considerably with the site and with the species of animal.

In the gastric mucosa of rats, guineapigs, and rabbits Williams (1953) found no evidence of re-formation of chief or parietal cells but only of crypts lined by mucus-secreting cells. Ferguson (1928), however, could find no evidence of regeneration of glands in the rabbit, whereas in the dog all elements of the gastric mucosa were re-formed. O'Connor (1954), who studied the healing of localised areas of necrosis in the colon of the mouse, found that, if the mucosa and the muscle layers were destroyed, the breach in the bowel wall became filled with granulation tissue, and adhesions were formed. In such areas regeneration of the mucosa was confined to the formation of an epithelial layer partially covering the damaged area; no new mucous glands were formed. Only when the bases of the crypts were left intact in the damaged area was the normal histological appearance regained.

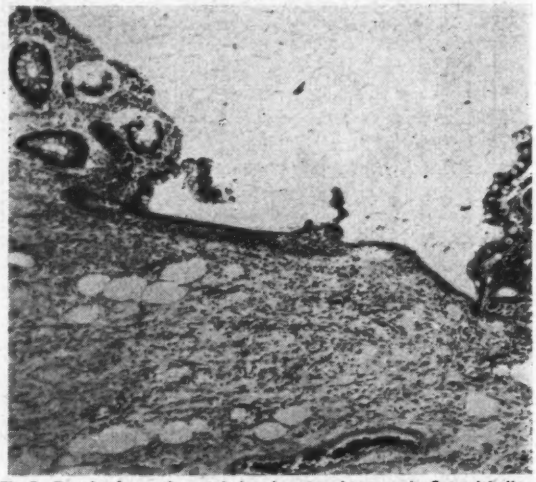


Fig. 5—Repair of experimental ulcer in normal mucosa by flat epithelium eleven days after trauma. (Hæmatoxylin and eosin. × 60.)

Our study of repair following surgical trauma in the rectum shows the following sequence of events. First the surrounding mucosal folds tend to fall over the denuded area, where granulation tissue is forming. On the third or fourth day after the trauma, flattened cells can be seen growing out from adjacent crypts, where the dividing cells in the base are undamaged. In one case after eleven days, in the absence of secondary infection, a small ulcer 2·5 mm. in diameter was completely covered by this

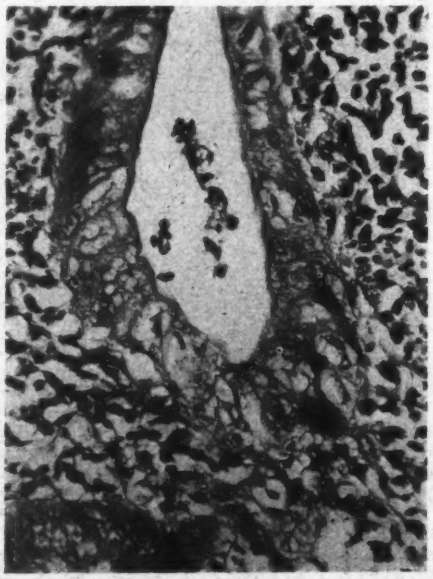


Fig. 6—Neutrophil infiltration of degenerate mucosal lining cells in ulcerative colitis. (Hæmatoxylin and eosin. × 280.)

epithelium (fig. 5). The underlying areas undergo fibrosis with consequent contraction. In these artificially induced ulcers there was no evidence of any tendency for the inflammation to spread beneath adjacent normal mucosa. On the contrary the process remained sharply localised.

When mucosal damage involves the entire crypt, surface repair will take place by an outgrowth from surrounding crypts, where actively dividing cells have been spared. It seems unlikely that these cells can form new crypts. Repeated trauma with resulting fibrous contraction and lack of new formation of crypts would inevitably lead to diminution of distensibility and to weakening of the mucosal barrier.

### Biopsy Material in Ulcerative Colitis

We studied 180 specimens from 150 cases of ulcerative colitis. In some cases the diagnosis had already been established, whereas in others the biopsy was used as one of the diagnostic procedures. The material used for this study comes from cases under careful review in the follow-up scheme at the Gordon Hospital. They are all

Fig. 7—Erosion showing rupture of crypt base in acute ulcerative colitis. (Hæmatoxylin and eosin. × 150.)

subjected to complete clinical scrutiny and full radiological and pathological investigations.

The correlation between histological appearances and clinical and sigmoidoscopic findings was accurate within certain limitations. In a few cases there was absence or quiescence of ulcerative colitis in the rectum with activity in a more proximal part of the colon, and in such circumstances no comparison was possible. Thirteen cases showed normal histological appearance in the rectal mucosa, and 3 showed quiescent appearances although symptoms and radiological changes suggested active ulcerative colitis elsewhere. In most cases the histological and sigmoidoscopic findings were in agreement. 11 cases, however, showed sufficient mucosal healing to produce a normal appearance on sigmoidoscopy and yet on microscopy showed characteristic histological changes.

### HISTOLOGICAL APPEARANCES IN ULCERATIVE COLITIS

Of the 180 specimens examined 119 showed evidence of active and 48 of quiescent ulcerative colitis. 3 biopsy specimens showed melanosis coli. In 2 specimens submucous granulomata were seen containing giant-cells

Fig. 8—"Crypt abscesses" in ulcerative colitis. (Hæmatoxylin and eosin. × 150.)

with no evidence of tuberculosis. Squamous metaplasia was not seen in any of the material of this series although it has been noted twice in operation specimens of the colon in ulcerative colitis.

*Active Ulcerative Colitis*

The earliest active lesion seems to develop in the bases of the crypts, where neutrophils are found passing between the lining cells to accumulate inside the lumen (fig. 6). The basal cells stain poorly. Their cytoplasm is vacuolated, and their nuclei show degenerative changes (fig. 6). As necrosis progresses, small erosions are produced which establish continuity between the lumen and the submucosa (fig. 7). The accumulation of neutrophils with eosinophils, red blood-cells, serum, and mucus in the lumen of the crypts constitutes the so-called "crypt abscess," which is a characteristic feature of ulcerative colitis (fig. 8). Excessive infiltration by eosinophils is inconstant at all stages; it was seen in a third of the cases in this series.

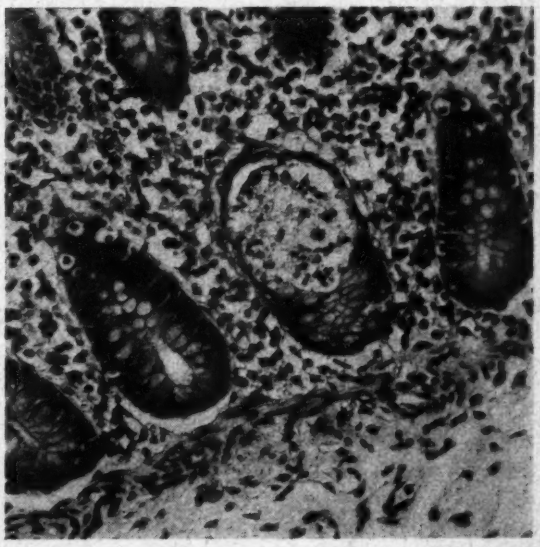


Fig. 9—Repair of partially damaged crypt in ulcerative colitis. (Hæmatoxylin and eosin. × 250.)

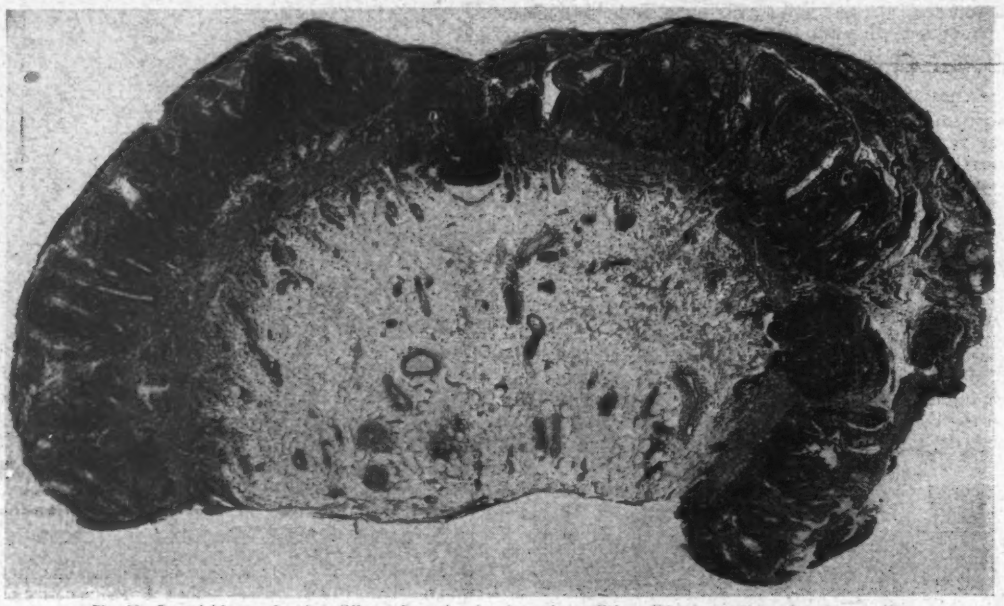


Fig. 10—Rectal biopsy showing diffuse ulceration in ulcerative colitis. (Hæmatoxylin and eosin. × 25.)

In the mildest lesions the destructive process may be limited to a portion of the crypt, and in such cases it is possible for repair by thin flattened epithelium to take place without loss of the normal architecture (fig. 9). More commonly, however, numerous crypts are involved, and large areas of their walls break down, liberating infective material into the submucosa and producing widespread ulceration. These ulcers are very rarely clear-cut. They usually present an irregular pattern of necrotic debris and inflammatory cells scattered among remaining fragments of viable epithelium (fig. 10). The inflammatory exudate shows neutrophils only in the most superficial areas. In the deeper zones lymphocytes and plasma-cells with smaller numbers of eosinophils predominate. An additional method of ulcer formation is by the spread of the inflammatory process in the submucosa, which strips off the overlying and relatively normal mucosa and produces the so-called "lacunal abscess" (fig. 11).

In most cases in this series (113 of the 119 active cases) ulcers were localised in depth at or above the level of the muscularis mucosæ. The cellular inflammatory exudate involved the submucosa more often. In our series 23 of the 167 abnormal biopsy specimens examined showed submucosal involvement, and they were all cases of long-standing ulcerative colitis. There is a small group of cases in which widespread involvement of the bowel wall with extensive muscle damage may occur early in the disease. Cases of this type have been reviewed elsewhere (Lumb et al. 1955).

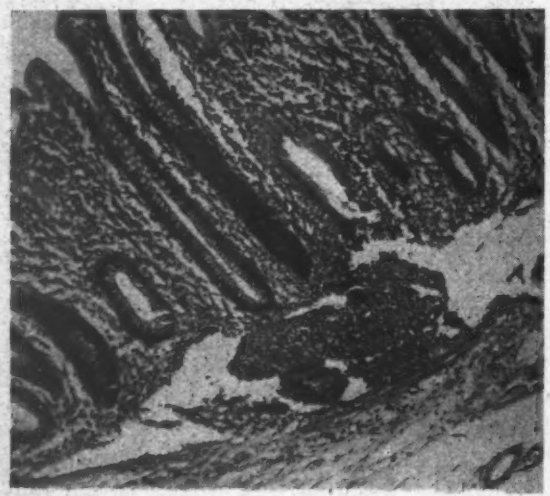


Fig. 11—"Lacunal abscess" in ulcerative colitis. (Hæmatoxylin and eosin. × 200.)

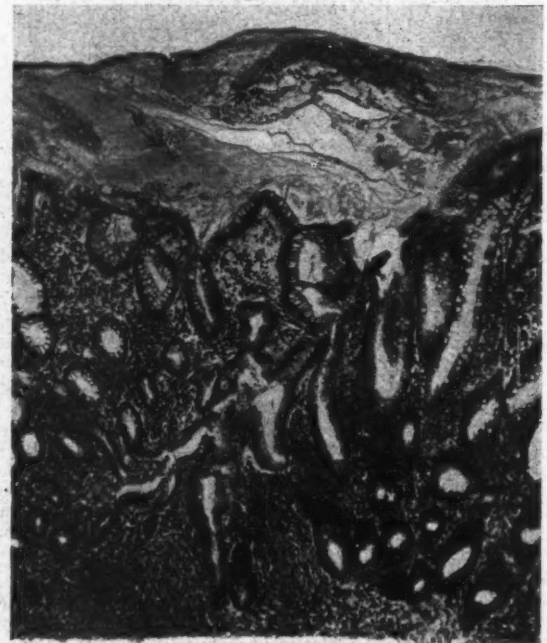


Fig. 12—Irregular structure and excessive secretion of mucus after repair in ulcerative colitis. (Hæmatoxylin and eosin. × 60.)

The intact cells in the surrounding epithelium differentiate to form increased numbers of goblet-cells. These cells pour out an excess of mucus, which coats the adjacent mucosa (fig. 12). The lamina propria is œdematous, and the capillaries are dilated and congested. Bleeding into the ruptured crypts and ulcerated areas is common.

The loss of continuity of the surface epithelium allows the normal intestinal flora to enter freely the submucosa and lamina propria. Seneca and Henderson (1950) found greatly increased numbers of coliforms and other normal intestinal bacteria in the stools in established cases of ulcerative colitis.

Damage and repair in the diseased areas tend to go hand in hand; so a single biopsy may show all stages from commencing progressive ulceration in one area to epithelial regeneration and repair in another. Vascular granulation tissue infiltrated by lymphocytes, plasma-cells, and eosinophils is formed in the damaged areas. Fibrous tissue is laid down which tends to contract and diminish the apparent size of the lesion. Epithelial regeneration takes place with the production of flattened

Fig. 13—Flattened epithelium growing over granulation tissue from adjacent surviving crypts in healing ulcerative colitis. (Hæmatoxylin and eosin. × 67.)

cells which grow out from adjacent surviving crypts (fig. 13).

These histological changes of active disease are completely correlated with the sigmoidoscopic appearances. Thus the earliest changes of erosions and small crypt abscesses are found in cases where congestion and loss of sheen are seen by the naked eye. In rectal biopsy material ulcers are smaller than those seen in operation specimens from the colon. This is partly because the biopsy specimen tends to be taken from a projecting fold of mucosa where there are no macroscopic ulcers, but it is also true that the large spreading ulcers seen in the colon are uncommon in the rectum.

Repair may be complete and the mucosa reconstituted. This state of quiescence may continue for varying periods without further activity. During this phase the symptoms may be mild and sigmoidoscopic appearances inconclusive. Granularity of mucosa and loss of distensibility are common during this period. Less often symptoms may disappear and sigmoidoscopic appearances become completely normal.

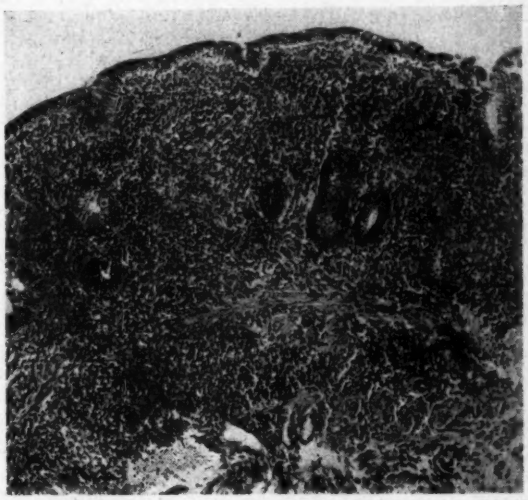


Fig. 14—Flattened but intact mucosa with lymphocytes and plasma-cells infiltrating muscularis mucosæ in ulcerative colitis. (Hæmatoxylin and eosin. × 67.)

*Quiescent Ulcerative Colitis*

It is at this stage that biopsy is of particular interest clinically, for abnormalities can be detected histologically.

The microscopic appearances show an intact mucosa with a considerably altered structural pattern. The change is always towards a diminution in the numbers of crypts and a generalised thinning following destruction during the ulcerative phase. This may be extreme (fig. 14) or less well marked (figs. 15 and 16). The regular arrangement of crypts, which is so characteristic of the healthy mucosa (fig. 3), is lost when repair takes place (fig. 12).

Goblet-cells are seen in larger numbers than normal (fig. 17), and the secretion of mucus is excessive (fig. 12).

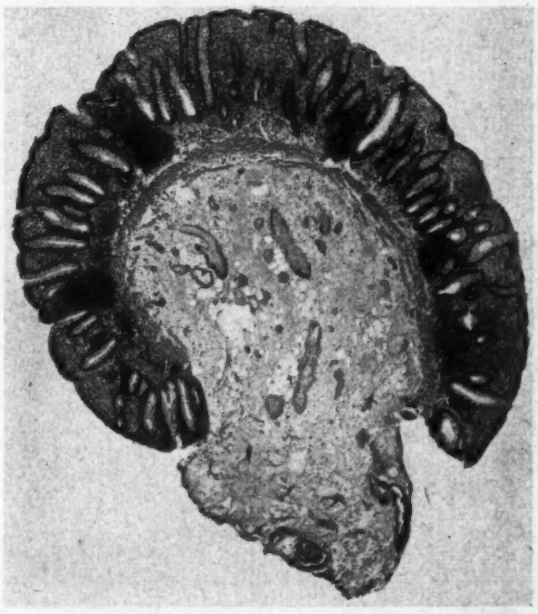


Fig. 15—Rectal biopsy showing intact irregular mucosa and follicular lymphoid hyperplasia in quiescent ulcerative colitis. (Hæmatoxylin and eosin. × 26.)

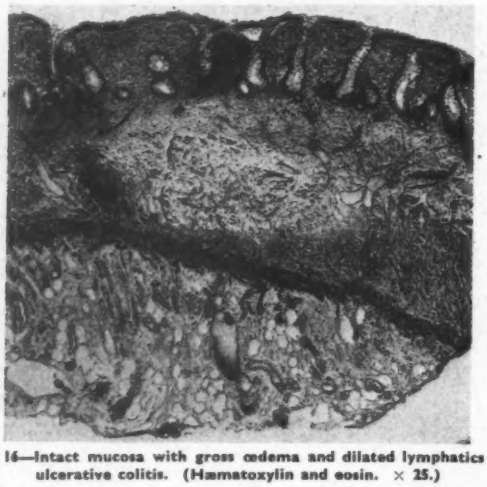


Fig. 16—Intact mucosa with gross œdema and dilated lymphatics in ulcerative colitis. (Hæmatoxylin and eosin. × 25.)

The cellular infiltration of the lamina propria and submucosa shows the following sequence of appearances. Immediately after an active phase dense accumulations of lymphocytes and plasma-cells are found lying below the newly healed epithelium (fig. 14). Often there is diffuse infiltration of the muscularis mucosæ by lymphocytes and plasma-cells, causing fragmentation of the muscle elements and making them appear "buried" in the cellular exudate (fig. 14). Large lymph follicles become apparent as the generalised cellular infiltration diminishes, and these are the cause of the "granularity" of the mucosa seen through the sigmoidoscope (fig. 15). Sheets of eosinophilic mucinous material are seen spread over the irregular mucosal surface (fig. 12). If the quiescent phase persists, lymphocytes gradually disappear, leaving grossly œdematous lamina propria and submucosa, with evidence of dilated lymph channels (fig. 16). Where the muscularis mucosæ has remained relatively intact it may be separated from the mucosa by this wide zone of œdematous connective tissue (fig. 16). Considerable numbers of young fibroblasts and capillaries are seen in this area, and fibrous tissue is gradually laid down (fig. 17). A small zone of ulceration may be healed and obliterated completely by fibrous tissue drawing together adjacent areas of mucosa which although abnormal have escaped complete destruction (fig. 18).

It must be emphasised that these various degrees of quiescence seen in the biopsy specimens give no indication of the subsequent course of the ulcerative colitis. Thus mucosal areas showing epithelial repair and relatively minor degrees of lymphocytic infiltration with œdema and fibrosis may at any time break down to produce fresh ulceration.

Fig. 17—Intact mucosa and submucosal fibrosis in quiescent ulcerative colitis. (Hæmatoxylin and eosin. × 84.)

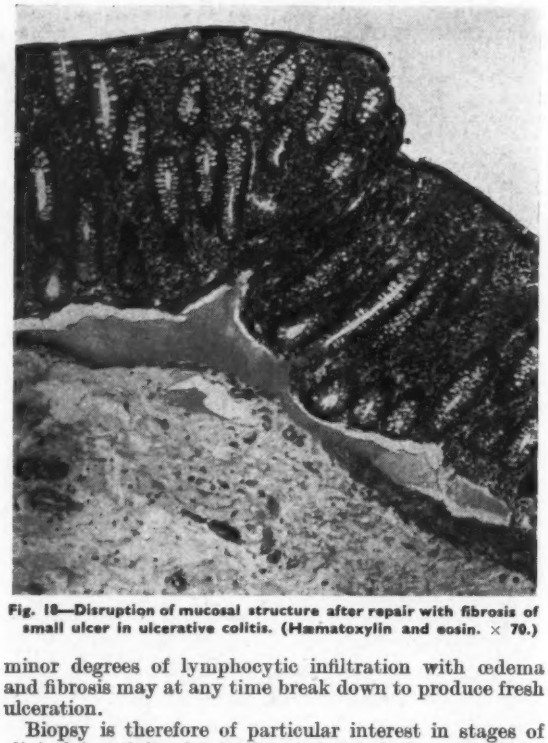


Fig. 18—Disruption of mucosal structure after repair with fibrosis of small ulcer in ulcerative colitis. (Hæmatoxylin and eosin. × 70.)

Biopsy is therefore of particular interest in stages of clinical inactivity for it shows that a lesion capable of renewed ulceration still exists. It is important to recognise these appearances of quiescent ulcerative colitis, for it then becomes possible to diagnose the disease even when no ulcers are present on examination.

## Discussion

The rectum is involved in many cases of ulcerative colitis. Of 150 cases in the present series 137 (91·4%) showed evidence of ulcerative colitis, and in 13 (8·6%) the biopsy specimens appeared normal. Of the 137 cases in which the rectum was involved 64 (46·7%) had radiological evidence of ulcerative colitis in the entire colon, whereas in 73 (53·3%) only the distal colon was affected. In 19 of these no radiological changes were found and the diagnosis was made by sigmoidoscopy and biopsy. In the remaining 54 cases radiological changes were seen in the sigmoid and/or in the descending colon.

Separate titles, such as idiopathic granular proctitis (Cropper 1955) and non-specific proctosigmoiditis (Brooke 1954), have been given to conditions localised in the distal colon and rectum. No histological evidence was found in this series to justify such a subdivision. It seems certain that none of the microscopic changes

described in ulcerative colitis is in any way specific, but the examination of biopsy specimens from 6 cases of non-specific diarrhœa revealed no histological abnormalities.

The primary lesion appears to consist of small erosions produced by breakdown of epithelial-cells at the bases of crypts, with subsequent formation of crypt abscesses and spread of the disease. In acute and severe cases widespread ulceration develops, but a chronic inflammatory exudate and some attempt at repair are nearly always seen. In milder cases the lesions remain more localised, the ulceration is not so severe, and repair is more obvious. In 48 cases (about a third of the present series) the mucosa was intact and the ulcerative colitis appeared to be quiescent.

Warren and Sommers (1949) suggested that a small proportion of cases of ulcerative colitis (19 of their 180 cases) resulted from mucosal degeneration following an inadequate blood-supply caused by necrosis and thrombosis of blood-vessels in the submucosa and mesentery as in polyarteritis nodosa. This condition they called "vasculitis." In the material examined in the present series there was no evidence of any proliferation of blood-vessels except in areas where there was sufficient active inflammation to cause secondary vascular change.

The essential lesion of ulcerative colitis seen in rectal biopsy material seems to be an excessive destruction of undifferentiated cells in the crypts, leading to failure of repair and to subsequent secondary infection. It therefore seems important to focus attention on the possible causes of degeneration and necrosis of these cells.

In the stomach the earliest lesions in gastritis develop at the neck of the crypts (Palmer 1954), and Wright (1954) says that the first changes in acute appendicitis take place in the depths of the mucosal folds. In both these regions the affected area is a zone of active division of undifferentiated cells, a fact which coincides with the findings in ulcerative colitis.

The mechanism of formation and rupture of crypt abscesses is of great importance in attempting to understand the ætiology of ulcerative colitis. Levine et al. (1951) suggest that ulcerative colitis is associated with an absence of the homogeneous ground-substance of the basement membrane of the epithelial-cells. They believe that abscesses can develop after rupture of the epithelium as a result of these changes. In this way the epithelium loses its barrier properties. Sommers et al. (1953) repeated this work by a different technique but could not detect any deficiency in this basement membrane, except locally in areas of inflammatory exudate. They concluded that basement-membrane "discontinuities" appear to be secondary to infiltration by leucocytes.

Warren and Sommers (1949) suggest that the crypts rupture from distension by pus-cells. They say that the cells lining the crypts are normal but become flattened as tension increases. In our study of this process gross distension of crypts sufficient to cause bursting was seen only rarely, whereas abnormality of the epithelial-cells was common. Serial sections cut through crypt-abscess areas revealed palely staining vacuolated cells undergoing necrotic change; actual breakdown of epithelial continuity; and foci of repair by flattened epithelial-cells.

It therefore seems reasonable to suppose that neutrophils are attracted by chemotactic influences originating either from the damaged cells or from organisms in the crypt lumina. Florey (1933) described essentially similar appearances after the introduction of pathogenic *Salmonella ærtrycke* into the mucosal crypts of the colon in guineapigs. Repeated searches, however, have revealed no primary causal organism in ulcerative colitis. Indeed until recently the more chronic cases were thought by some observers to be chronic bacillary dysentery. This view was favoured by Hurst (1921), Felsen (1945), Stewart (1950), and Felsen and Wolarsky (1953).

Difficulty in isolating a dysenteric organism in ulcerative colitis cannot be explained by lack of a suitable technique, and Felsen's evidence that dysentery may precede ulcerative colitis and regional ileitis is not convincing. Bargen's "bacillus" is now regarded as a commensal diplostreptococcus. Cropper (1955) emphasises that many patients with idiopathic granular proctitis have been hastily and uncritically diagnosed as having some form of tropical dysentery and treated as such. We agree with Warren and Sommers that any attempt to isolate cases of ulcerative colitis from those of non-specific diarrhœa previously published is impossible in retrospect.

Other ætiological factors have been suggested to account for the death of mucosal cells. Very briefly these are as follows:

(1) An allergic inflammatory origin (Andresen 1942, 1949).
(2) Parasympathetic hyperactivity, which may originate from psychogenic stimuli (Grace et al. 1950). Muscular spasm (Lium 1939) and vascular dilatation mediated through parasympathetic agents (Wener et al. 1949) have both been shown experimentally to cause colonic ulceration.
(3) Some local surface irritant of enzymatic type—e.g., mucinase (Sammons 1951).

None of these theories has proved adequate. Most of the experimentally produced ulcerative lesions in the colon are transient and do not produce lesions truly resembling human ulcerative colitis. It may well be therefore that no single cause exists, but that some intrinsic failure of normal regeneration of epithelial-cells may be aggravated by several extrinsic factors.

## Summary

The histological appearances of 100 biopsy specimens of normal rectal mucosa were studied.

The healing of healthy rectal mucosa after trauma was examined and is discussed.

180 biopsy specimens from 150 cases were investigated. In 137 of these cases disease of the rectum was found.

The early lesions of ulcerative colitis are described, and the mechanism of their formation is discussed.

Of the 180 specimens 48 (26·7%) were in a quiescent phase clinically. Their histological appearances are described and the use of biopsy in the diagnosis of this group is discussed.

Our thanks are due to the members of the medical and surgical staff of the Gordon Hospital for their collaboration in providing the surgical material for this study, especially Mr. G. S. Ramsay, who did most of the biopsies; Mr. J. R. Stokes for his technical assistance; and Mr. E. V. Willmott for some of the photomicrographs. One of us (R. H. B. P.) was assisted by a grant from the Westminster Hospital Board of Governors Discretionary Fund.

### REFERENCES

Andresen, A. F. R. (1942) *Amer. J. digest. Dis.* **9**, 91.
— (1949) *N. Y. St. J. Med.* **49**, 1783.
Brooke, B. N. (1954) Ulcerative Colitis and its Surgical Treatment. Edinburgh.
Cropper, C. F. J. (1955) *Lancet*, i, 1253.
Dukes, C. E., Bussey, H. J. R. (1926) *J. Path. Bact.* **29**, 111.
Felsen, J. (1945) Bacillary Dysentery, Colitis and Enteritis. Philadelphia.
— Wolarsky, W. (1953) *J. Amer. med. Ass.* **153**, 1069.
Ferguson, A. N. (1928) *Amer. J. Anat.* **42**, 403.
Florey, H. W. (1932) *Brit. J. exp. Path.* **13**, 349.
—, (1933) *J. Path. Bact.* **37**, 283.
Gabriel, W. B., Dukes, C. E., Bussey, H. J. R. (1951) *Brit. J. Surg.* **38**, 401.
Grace, W. J., Wolf, S., Wolff, H. G. (1950) *J. Amer. med. Ass.* **142**, 1044.
Hurst, A. F. (1921) *Guy's Hosp. Rep.* **71**, 26.
Levine, M. D., Kirsner, J. B., Klotz, A. P. (1951) *Science*, **114**, 552.
Lium, R. (1939) *Arch. intern. Med.* **63**, 210.
Lumb, G. D., Protheroe, R. H. B., Ramsay, G. S. (1955) *Brit. J. Surg.* **43**, 182.
O'Connor, R. J. (1954) *Brit. J. exp. Path.* **35**, 545.
Palmer, E. D. (1954) *Medicine, Baltimore*, **33**, 199.
Sammons, H. G. (1951) *Lancet*, ii, 239.
Seneca, H., Henderson, E. (1950) *Gastroenterology*, **15**, 34.
Sommers, S. C., Anderson, L. M., Warren, S. (1953) *Lab. Invest.* **2**, 223.
Stewart, G. T. (1950) *Brit. med. J.* i, 405.
Warren, S., Sommers, S. C. (1949) *Amer. J. Path.* **25**, 657.
Wener, J., Hoff, H. E., Simon, M. A. (1949) *Gastroenterology*, **12**, 637.
Williams, A. W. (1953) *Brit. J. Surg.* **41**, 319.
Wright, G. P. (1954) An Introduction to Pathology. London.

# THE ELECTRON-MICROSCOPY OF ATHEROMA*

C. I. LEVENE
M.D. Lond.
*From the Department of Pathology, Royal Victoria Infirmary, Newcastle upon Tyne*

*With illustrations on plate*

DURING the past nine years Duguid has put forward the thesis that atherosclerosis as we know it in man is largely the product of thrombosis (Duguid 1946, 1948, 1949, 1952, 1954, 1955, Duguid and Robertson 1955). He suggests that the fibrous tissue which forms the atherosclerotic plaque, although it gives all the staining reactions ascribed to collagen, is actually fibrin and represents mural thrombi which, having been covered by endothelium, are incorporated in the vessel walls and then packed down by the pressure of the blood.

To test this suggestion I examined typical plaques by electron-microscopy. The electron-microscopic structures of collagen and fibrin are quite distinctive, and it seemed likely that a clear identification could be made by comparing known samples of these with the material in question. The results strongly support Duguid's suggestion.

## Methods and Materials

Tissues to be examined by electron-microscopy were teased and minced in distilled water, and suspensions of them were washed twice by centrifuging. A drop of the suspension was then placed on an electron-microscopic specimen grid which had been previously covered with a thin 'Formvar' membrane, and the drop was allowed to dry in air. After two hours' further drying in a high vacuum the grid was shadowed with gold-palladium metal at an angle of 2 : 1 and scanned in the electron-microscope for at least half an hour. Four grids were prepared from each specimen, and from four to eight representative fields photographed at a magnification of 11,300. Further enlargements to 67,800 were then made photographically. The electron-microscope used was a Metropolitan-Vickers type E.M.3, with an adjustable objective aperture (50 μ) and a × 10 telescopic attachment. Unshadowed specimens of collagen and fibrin were also examined after having been treated for fifteen minutes with a 0·2% solution of phosphotungstic acid. Most of the tissues were fixed in formalin, it having been ascertained that fixation did not materially affect the periodicity measurements of collagen or fibrin.

*Collagen*

Standard examples of normal collagen were obtained from human tendo achillis (fig. 1), chordæ tendiniæ of the heart from various age-groups, portions of dermis, a surgically removed fibroma of the jaw, and a portion of the tail tendon of a rat.

The characteristic electron-microscopic features of mammalian collagen are a transverse periodicity of about 640 Å (1 μ = 10,000 Å), and a fibre width of 350–800 Å. The fibres are easily recognisable on the electron-microscope screen by using the telescopic attachment.

*Fibrin*

Standard examples of fibrin were prepared by adding calcium-chloride solution to human plasma.

The characteristic features of fibrin (fig. 2) are a beading of the fibres in shadowed specimens, with a regular periodicity of about 230 Å. In a freshly formed clot the fibres are considerably thinner than those of collagen (less than 100 Å thick) and can therefore be recognised only in the enlarged photographs.

A comparison of unshadowed preparations of collagen (fig. 3) and fibrin (fig. 4) shows the striking difference in their periodicities.

*Intimal Plaques*

Fifteen aortas were selected at random, and from each an atheromatous plaque was taken and bisected longitudinally, half being used for ordinary histology and half for electron-miscroscopy. Histological sections were stained with hæmatoxylin and eosin, Van Gieson, and Lendrum's (1949) acid picro-Mallory. All gave the staining reactions commonly ascribed to collagen, but in addition, with the acid picro-Mallory stain, seven of the plaques showed masses of fibrinous material lying either superficially or in the deeper layers of the thickened intima. In the other eight no fibrin staining was seen. From the remaining half of each plaque a portion of the intima was separated under the dissecting microscope and prepared for electron-microscopy in the usual way.

The findings, which were practically constant, showed that in each of the plaques, including those devoid of stainable fibrin, there was a preponderance of fibres which did not in the least resemble collagen but had the periodicity more characteristic of fibrin (fig. 5)—i.e., about 230 Å—and a fibre width of 250–400 Å. In six of the plaques no collagen at all was observed, and in the remaining nine such collagen as was present comprised only about 5% of all the fibres present.

I then decided to examine the different levels of an average intimal plaque, and for this purpose five specimens were selected, each of which gave in ordinary histological sections the staining reactions for "collagen" only. From each plaque successive layers about 1 mm. in thickness were stripped away under the dissecting miscroscope and examined individually. From two to six layers were taken, according to the thickness of the plaque, and in two instances part of the media also was included.

The electron-microscopic appearances were again quite constant, the superficial layer consisting of fine fibres, about 100 Å thick, with a regular beading of periodicity 230 Å, and the deeper layers (fig. 6) consisting of slightly thicker fibres (250 Å) but with the same periodicity. The appearance was in fact identical with that seen in the fifteen plaques previously examined. The fibres of the media, on the other hand, consisted mainly of collagen (periodicity 640 Å), the more delicate muscle having been destroyed in the preparation.

*Trypsin Digestion*

Fresh fibrin is digested by trypsin, whereas collagen remains virtually unaffected. I therefore decided to

* Read at a conference of the Pathological Society of Great Britain in July, 1955.

## LEGENDS TO ILLUSTRATIONS ON PLATE

DR. LEVENE

**Fig. 1**—Collagen fibre from human tendo achillis, showing characteristic periodicity of 640 Å. (Shadowed with gold-palladium. × 67,800.)

**Fig. 2**—Human fibrin, showing fibrils with characteristic beading of periodicity 230 Å. (Shadowed with gold-palladium. × 67,800.)

**Fig. 3**—Collagen fibre from human tendo achillis, showing periodicity of 640 Å. (Unshadowed, stained with phosphotungstic acid. × 67,800.)

**Fig. 4**—Bundles of human fibrin fibrils, showing periodicity of 230 Å. (Unshadowed, stained with phosphotungstic acid. × 67,800.)

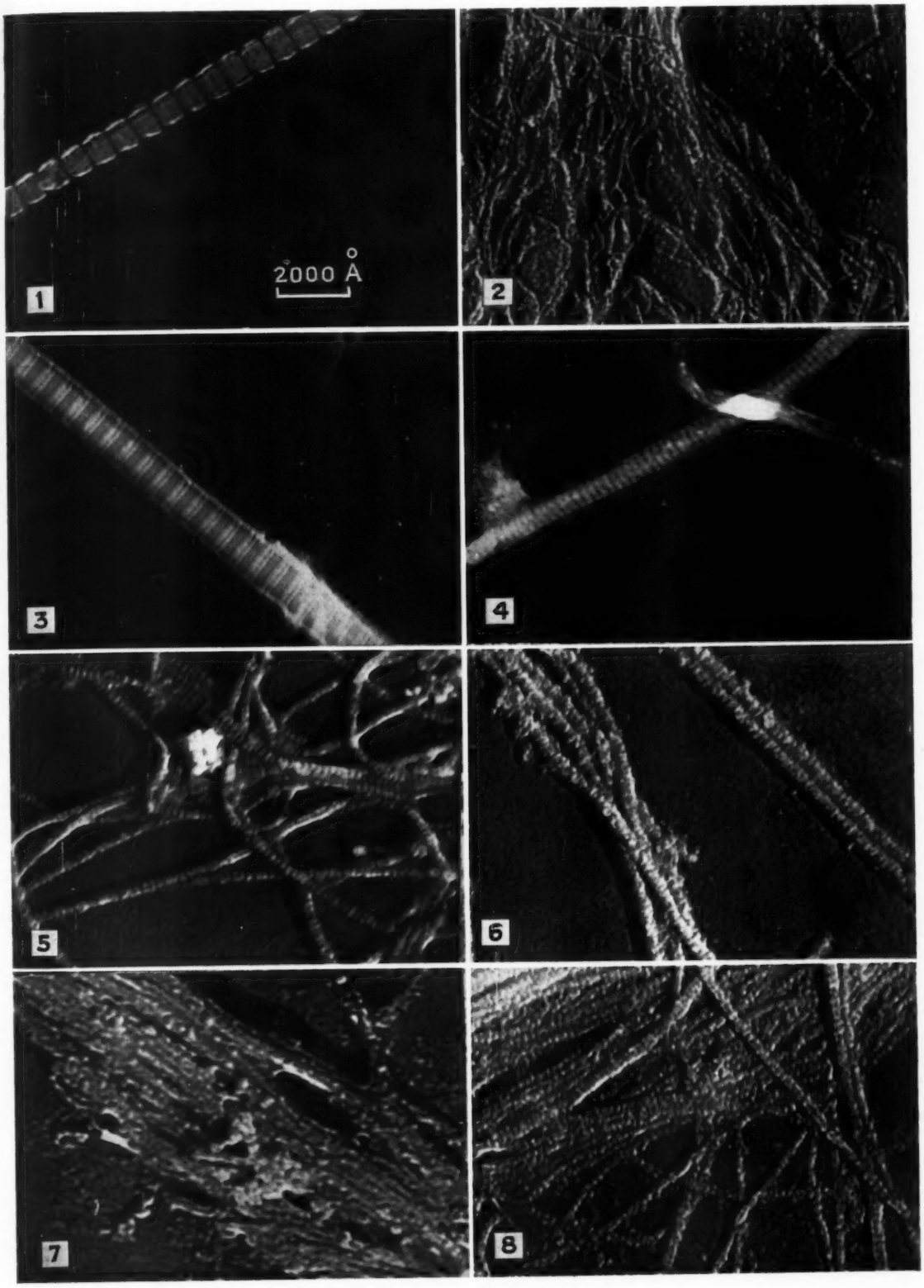
**Fig. 5**—Fibres from aortic intimal plaque, showing periodicity of about 230 Å. (Shadowed with gold-palladium. × 67,800.)

**Fig. 6**—Fibres from intima of atheromatous plaque, showing periodicity of about 230 Å. (Shadowed with gold-palladium. × 67,800.)

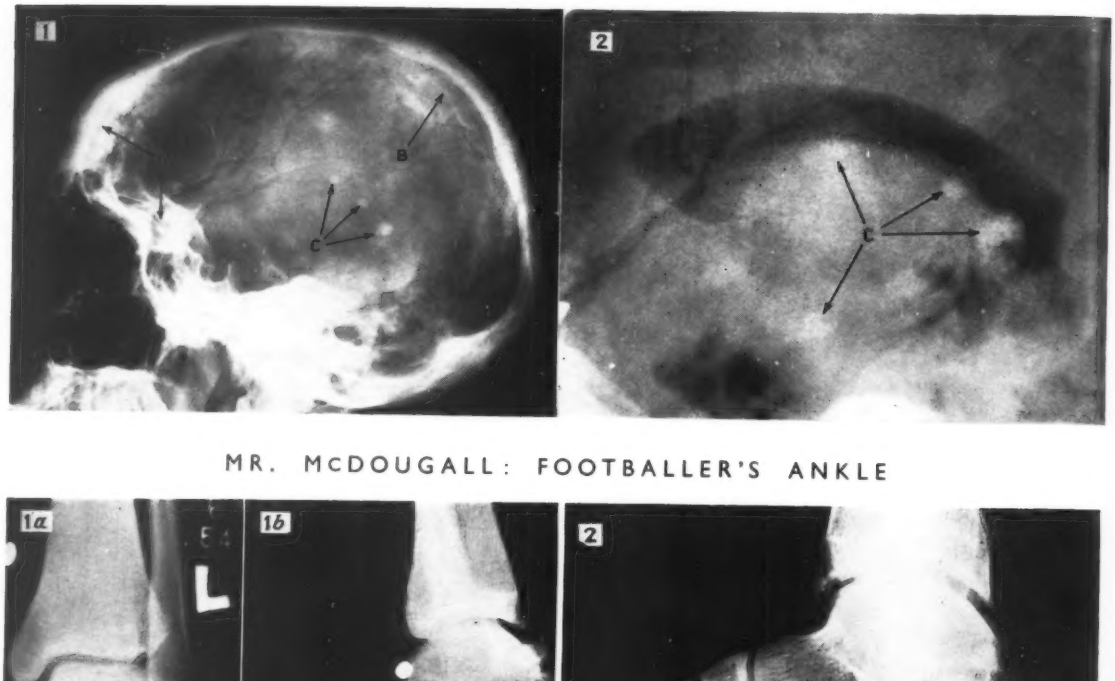
**Fig. 7**—Superficial fibres from normal aortic intima. These are indistinguishable from fibrin. (Shadowed with gold-palladium. × 67,800.)

**Fig. 8**—Deep fibres from normal aortic intima. Although they are slightly thicker, their periodicity is the same as that of fibrin, 230 Å. (Shadowed with gold-palladium. × 67,800.)

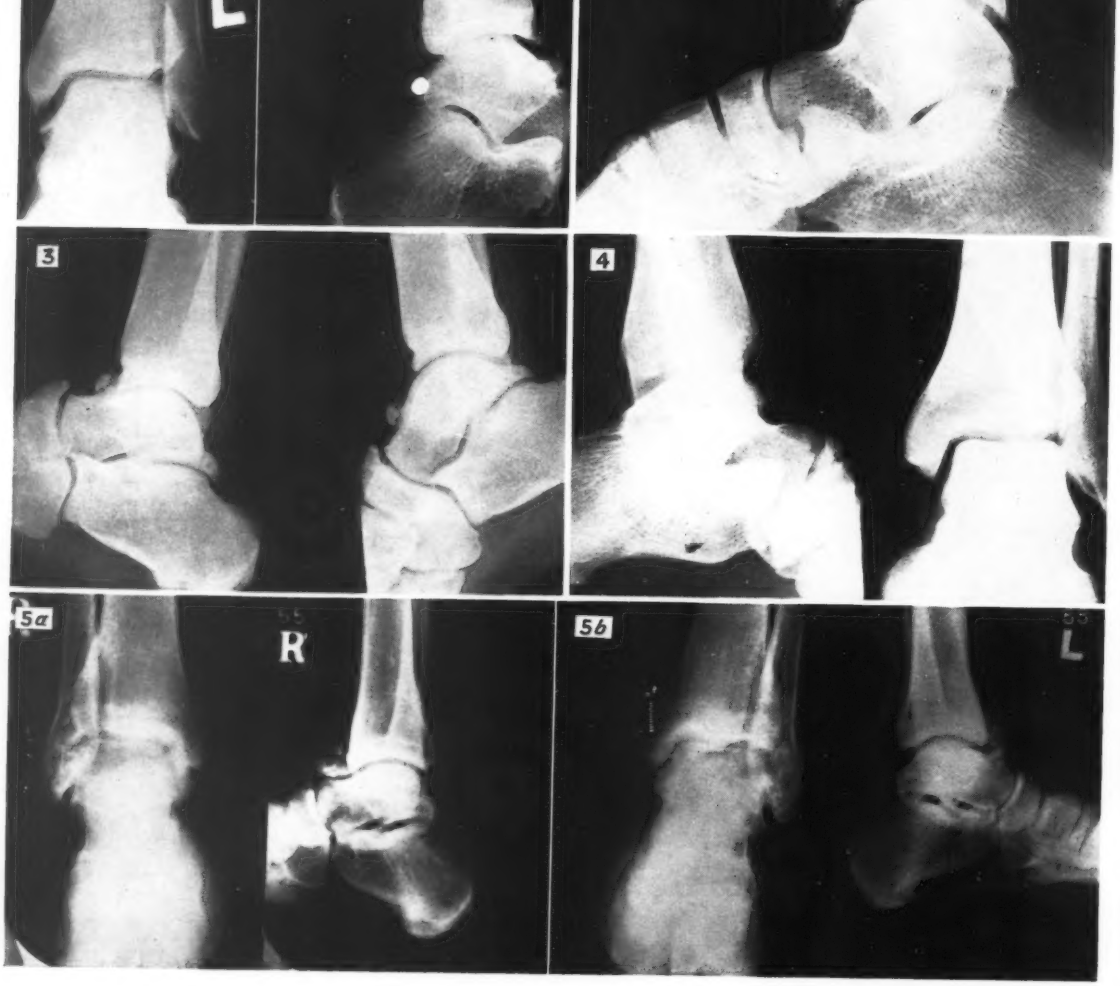
DR. LEVENE: ELECTRON-MICROSCOPY OF ATHEROMA



## DR. LUCAS AND DR. DAVIS: TUBEROUS SCLEROSIS




## MR. McDOUGALL: FOOTBALLER'S ANKLE



try the effect of trypsin on the fibres from an intimal plaque. A pilot experiment established that, whereas a fresh fibrin clot treated with a 0·1% solution of chymotrypsin at 37°C for two hours is completely digested, a formalin-fixed clot similarly treated is more resistant. When a suspension of the 230 Å fibres from a formalin-fixed intimal plaque was treated with chymotrypsin, a definite but only partial digestion had taken place after two hours, suggesting that these fibres are fibrinous.

*Normal Intima*

Finally the electron microscopic structure of an apparently normal aortic intima was examined. Five normal-looking aortas were selected at random, the youngest a year old, and the oldest sixty-five years old. A strip of aorta was taken from each, and half the area of intima was scraped away in two layers with a knife-blade, histological preparations being subsequently made as a check on the amount of tissue removed. In none of the specimens was collagen found, the fibres in all cases being identical with those in the atheromatous plaques (230 Å); but, whereas those of the superficial layer (fig. 7) were of about the same thickness as fresh fibrin, those in the deeper layer (fig. 8) were on the whole slightly thicker (200 Å).

## Discussion

The striking thing that emerges from these experiments is the confirmation of a long-held suspicion that the different forms of connective tissue cannot be identified by their staining reactions. Baitsell's (1916) argument that fibrin is the source of the connective tissue formed in the healing of wounds is upheld. It therefore appears that fibrin must be admitted as a form of connective tissue. Furthermore the electron-microscopical evidence supports the hypothesis put forward by Duguid (1946) and confirmed by Crawford and Levene (1952) that fibrin is deposited from the blood-stream and incorporated into the intima of arteries to produce fibrous thickening indistinguishable from atherosclerosis. These findings, as Duguid suggested (1952), strike at the roots of the "cellular theory," for not only do they indicate that atheromatous plaques thicken by fibrinous encrustation but also they suggest that the same mechanism operates even in the normal development of the human aortic intima.

## Summary

Human atheromatous plaques, which under the light-microscope give the staining reactions acribed to collagen, are found under the electron-microscope to consist mainly of fibrin.

The same appears to hold true for the normal aortic intima.

I wish to thank Prof. J. B. Duguid, who suggested this work; Dr. A. L. Latner for helpful advice and supplies of chymotrypsin; Miss Greta Joyce for her assistance with the histological preparations; and Mr. E. H. Boult, B.SC., of the chemistry department, King's College, University of Durham, for coöperation with the electron-microscopy and photography.

REFERENCES

Baitsell, G. A. (1916) *J. exp. Med.* **23**, 739.
Crawford, T., Levene, C. I. (1952) *J. Path. Bact.* **64**, 523.
Duguid, J. B. (1946) *Ibid*, **58**, 207.
— (1948) *Ibid*, **60**, 57.
— (1949) *Lancet*, ii, 925.
— (1952) *Ibid*, ii, 207.
— (1954) *Ibid*, i, 891.
— (1955) *Brit. med. Bull.* **11**, 36.
— Robertson, W. B. (1955) *Lancet*, i, 525.
Lendrum, A. C. (1949) *J. path. Bact.* **61**, 443.

## LEGENDS TO ILLUSTRATIONS ON PLATE

DR. LUCAS AND DR. DAVIS

**Fig. 1—Lateral view of skull showing (A) thickening of frontal bone extending into the floor of the anterior fossa, (B) sinuous calcification in the parietal region, (C) intracranial calcified nodules.**

**Fig. 2—Air encephalogram demonstrating calcified nodules projecting from the floor of the lateral ventricle (C).**

MR. McDOUGALL

**Fig. 1—Left ankle of a footballer of 24: (*a*) in the anteroposterior view, bone formation is present below the medial malleolus; (*b*) the lateral view shows bony outgrowths from the tibial margin and neck of the astragalus, and loose bodies are present behind the joint. (The round white spot in (*b*) is an artefact.)**

**Fig. 2—Right ankle of a footballer of 20. Bony outgrowths present along anterior and posterior tibial margins. Ankle-joint movements were considerably restricted here.**

**Fig. 3—Right ankle of a footballer of 24. Bony outgrowths along the tibial margin and neck of astragalus (*a*) come into contact on dorsi-flexion (*b*). The peculiar beaking of the navicular occurs when strain falls on the mid-tarsal joint.**

**Fig. 4—Left ankle of a goalkeeper of 20 showing characteristic fracture of the navicular.**

**Fig. 5—(*a*) Right and (*b*) left ankles of a professional circus artist of 27. Numerous loose bodies are present in the ankle-joint. There is marginal lipping of the tibiæ and beaking of the upper margins of both naviculars. In the anteroposterior views ossification can be seen in the collateral ligaments.**

# TUBEROUS SCLEROSIS
## WITH INVOLVEMENT OF THE CERVICAL CORD

C. J. LUCAS
M.B. Lond., M.R.C.P.
MEDICAL REGISTRAR

S. DAVIS
M.B. Lond., M.R.C.P.
SENIOR REGISTRAR

*From the Departments of Neurology and Diagnostic Radiology, University College Hospital, London*

*With illustrations on plate*

TUBEROUS SCLEROSIS is the result of a developmental anomaly of unknown cause; it may be familial or hereditary and it is not known to be associated with any biochemical abnormality. The essential pathological change is the occurrence of nodules in the brain, and with these, cutaneous lesions such as adenoma sebaceum, shagreen patches, and subungual fibromata are often found. Other sites of defective development or of tumour formation include the retina, kidney, heart, lungs, thyroid, thymus, adrenal, and ovary.

The general features of the disease have been reviewed by Critchley and Earl (1932), by Ross and Dickerson (1943), and by Dawson (1954), who discusses in particular the pulmonary changes. The classical features of idiocy, epilepsy, and adenoma sebaceum may vary greatly from case to case, and when the development of symptoms is incomplete or postponed until adult life the diagnosis may be difficult. Thus Stewart (1935) described the case of a woman of 21 who appeared healthy in all other ways when she died suddenly in status epilepticus. At necropsy the diagnosis was made by the discovery of numerous cerebral nodules, but none of the other stigmata of tuberous sclerosis were found.

The diagnostic importance of the radiological changes in the skull and bones has been recognised only comparatively recently. Thus, although Hall (1940) regarded bone changes as extremely rare, Sutton and Liversedge (1951), reviewing the literature, draw attention to their diagnostic value, and Berland (1953), agreeing, estimates that they are present in 60–65% of cases. The most characteristic changes are those in the skull, which may show intracranial calcification of various types. This is said to be almost pathognomonic if it is in the form of small, discrete, multiple opacities; but a sinuous type of calcification may also occur, and the vault of the skull may show mottling or thickening. The presence of intraventricular nodules, revealed by air encephalography,

provides valuable confirmatory evidence of the diagnosis. In the hands and feet one or more of the following may be seen: cyst formation, periosteal thickening, and osteoporosis. In the long bones there may be fibrocystic changes or small periosteal nodules. If adenoma sebaceum is present, histological examination of skin removed by biopsy may yield important confirmation of the diagnosis during life. Electro-encephalographic changes occur but they are non-specific (Dickerson and Hellman 1952).

In the following case the clinical features were atypical and the diagnosis was first suggested and later confirmed by the radiological findings alone.

## Case-report

A builder's labourer, aged 22, was admitted to University College Hospital in November, 1954, under the care of Dr. Blake Pritchard, by the courtesy of Dr. J. A. Cardno of the Hackney Hospital, from whom he had first sought advice.

*History*

He had complained of weakness and wasting of the right hand and arm for 2 years. The disability had been slight at first, and difficulty in handling a rifle while in the Army was the initial symptom. On his discharge from the Army the symptoms had become more obvious, but he was able to work as a builder's labourer until the time of his admission. He had in addition noted occasional pain in the left side of his face during several periods of a few days. Although he had not noticed any change in his appearance, his father had commented recently on the prominence of the right side of his forehead. He had had no epileptic attacks of any form. Following measles in childhood, he had been left with a squint in the left eye, which had been corrected operatively a year previously.

His parents, his brothers (aged 16 and 26), and one sister (aged 24) are all in good health. One sister aged 9 is a mongol. No relatives have suffered from epilepsy.

*Examination*

He was a well-built, healthy looking man, with prominence of the forehead on the right side. There was some asymmetry of the chest, the right side appearing fuller than the left, but no other skeletal abnormality was noted clinically. In the nervous system there were a well-developed right Horner's syndrome, impairment of the left corneal reflex, and wasting of the right side of the tongue. The right arm showed wasting of the distal third of the forearm and of the thenar eminence, with weakness of abduction and opposition of the thumb and of flexion of the wrist. The tendon reflexes were sluggish in both arms. There was slight impairment of all forms of sensitivity at the ends of the first, second, and third fingers of the right hand. The abdominal responses were impaired on both sides. In the legs the power was normal but the tone was increased; the reflexes were very brisk, more so on the right. The right plantar response was extensor. Apart from impairment of vibration in both legs, sensitivity was normal.

His heart, lungs, and abdomen were normal.

Dr. W. N. Goldsmith reported that there were no spots characteristic of adenoma sebaceum on the face. There was a probable sebaceous cyst on the right cheek and a cellular nævus on the left, but portions removed for biopsy showed no sign of adenoma sebaceum (Dr. P. J. Hare).

*Psychological Testing* (Miss G. Rawlings)

Wechsler-Bellevue Intelligence Scale. Form I. Verbal scale I.Q. 100. Performance scale I.Q. 96. Full scale I.Q. 98. Conclusion: a man of average intelligence, with no evidence of intellectual deterioration.

*Investigations*

Hæmoglobin 115%. White blood-cells 6800 per c.mm. Erythrocyte-sedimentation rate 3 mm. in 1 hour. Wassermann reaction and Kahn test negative. Serum-calcium 10·1 mg. per 100 ml. Plasma inorganic phosphorus 3·5 mg. per 100 ml. Plasma alkaline phosphatase 6·6 units per 100 ml. (King). Cerebrospinal fluid: pressure 137 mm.; free flow; normal rise and fall to jugular compression; white cells 1 per c.mm.; Pandy's test negative; protein 30 mg. per 100 ml.; chlorides 720 mg. per 100 ml.; sugar normal; Wassermann reaction negative; Lange curve 0000000000. Renal function: concentration and dilution test 1002–1022; urea-clearance (1) $C_M$=60%, (2) $C_M$=84%. Urine: standard amino-acid chromatogram; normal "glycine-taurine" pattern (Dr. C. E. Dent).

The electro-encephalogram was slightly abnormal. The alpha rhythm was of lower voltage in the left temporal area than the right, and there were occasional runs of low-voltage fast activity in the left central region (Dr. J. Foley).

*Radiological Findings*

The chest was normal The skull was shown to be thickened, particularly in the frontal region, where the changes extended into the floor of the anterior fossa (fig. 1). There was intracranial calcification of two types: (1) sinuous, visible near the sagittal plane in the parietal region; and (2) nodular, seen on the left side in the parietal region. In the pelvis the ischial bones showed a punctate increase in density. The hands and feet were normal.

A lumbar air encephalogram revealed three small calcified nodules protruding into the left lateral ventricle and another in the left frontal horn. A further calcified nodule probably lay partly within the temporal horn (fig. 2). A complete spinal myelogram by lumbar route was normal.

Radiographs of skulls, chests, and hands of his parents and his two sisters aged 9 and 24 showed none of the changes of tuberous sclerosis.

## Discussion

The diagnosis of tuberous sclerosis in this case rests on the radiological findings. The occurrence of multiple discrete calcified nodules, some of which project into the lateral ventricles, has not been demonstrated in any other condition, and the thickening of the skull vault and the sinuous type of intracranial calcification, are also recognised features.

The punctate increase in density seen here in the ischial bones has not previously been described. Its appearance is not unlike that of the larger discrete areas of increased density sometimes seen in skull vault—noted particularly by Holt and Dickerson (1952)—and it may prove in other cases to be a radiological finding of diagnostic significance.

Thickening of the skull in tuberous sclerosis was noted at necropsy by Sailor (1898) and by Lind (1924). Perusini (1905) noted asymmetry of the skull clinically in one case, and palpable irregularity of the calvarium was observed by Budenz (1950) in a 38-year-old man with tuberous sclerosis. The prominence of the right frontal region in our case had been noticed by the patient's father.

The disease rarely produces localised neurological disturbance, although monoplegia, hemiplegia, paraplegia, or tetraplegia, and occasionally signs of cerebellar disorder, may occur when there are intracranial nodules, or gliomatous masses. Hydrocephalus also has been noted. Therefore the conspicuous disturbance of the spinal cord in this case is of special interest.

Spinal-cord involvement was noted by Perusini (1905), who described one case in which the cord at necropsy showed patchy diffuse changes, and referred to another, described by Pellizi (1901), in which there was gliosis of the white matter with nodule formation, the changes being most conspicuous in the cervical region. Clinical abnormality was recorded only in the last case in which, although it was stated that the motor abnormality in the upper limbs was greater than in the lower, further details are not known; for Pellizi's original communication has not been traced.

The spinal cords of two of the cases described by Ross and Dickerson were also abnormal; one from a woman of 20 showed scattered heterotopic and atypical cells, and the other from a boy of 4 showed diffuse glial proliferation in the posterior columns. No clinical observations of cord disturbances were included in these cases.

In the present case the neurological disturbances are entirely atypical: there is no mental impairment, no epilepsy, no significant cutaneous abnormality, and no relevant family history. On the other hand, there is not only a well-developed lesion of the cervical part of the spinal cord but also evidence of damage of two cranial nerves—slight in respect of the trigeminal, and gross in respect of the hypoglossal. No probable alterna-

tive explanation of these cranial-nerve affections can be suggested, but for the localised damage of the cervical cord other causes are possible though unlikely. A neurofibroma or other extramedullary lesion, with root involvement and cord compression, can be reliably excluded by the completely normal myelogram, and the composition and pressure responses of the cerebrospinal fluid. Syringomyelia is known to be associated occasionally with other developmental abnormalities, and must be considered; but the absence of any dissociated sensory loss in the presence of well-marked cord damage would be highly unusual, although not altogether incompatible with syringomyelia (Kinnier Wilson 1954). Therefore, it is suggested that the neurological changes in this case are an unusual manifestation of tuberous sclerosis.

### Summary

A case of tuberous sclerosis in a man of 22 years is described and discussed. The radiological findings, upon which alone the disease was identified, are described. The clinical picture, from which the usual features of this disease were absent, was one of damage to cranial nerves and cervical cord.

We wish to thank Dr. Blake Pritchard for permission to publish this case, and for his advice. We are also indebted to Dr. S. Cochrane Shanks and Dr. C. J. Hodson, of the department of radiology, University College Hospital, and to Dr. Hugh Davies of the National Hospital, Queen Square, for their assistance.

#### REFERENCES

Berland, H. I. (1953) *Arch. Neurol. Psychiat., Chicago*, **69**, 669.
Budenz, G. C. (1950) *Radiology*, **55**, 522.
Critchley, M., Earl, C. J. L. (1932) *Brain*, **55**, 311.
Dawson, J. (1954) *Quart. J. Med.* **9**, 1.
Dickerson, W. W., Hellman, L. (1952) *Neurology*, **2**, 248.
Hall, G. S. (1940) *Quart. J. Med.* **9**, 1.
Holt, J. F., Dickerson, W. W. (1952) *Radiology*, **58**, 1.
Kinnier Wilson, S. A. (1954) Neurology. London.
Lind, W. A. T. (1924) *Med. J. Aust.* ii, 290.
Perusini, G. (1905) *Mschr. Psychiat. Neurol.* **17**, 169, 255, 352.
Ross, A. T., Dickerson, W. W. (1943) *Arch. Neurol. Psychiat., Chicago*, **60**, 233.
Sailor, J. (1898) *J. nerv. ment. Dis.* **25**, 402.
Stewart, R. M. (1935) *Brit. med. J.* ii, 60.
Sutton, D., Liversedge, L. A. (1951) *J. Fac. Radiol., Lond.* **2**, 224.

## FOOTBALLER'S ANKLE

A. McDOUGALL
M.B. Glasg., F.R.C.S.E., F.R.F.P.S.
ASSISTANT ORTHOPÆDIC SURGEON, ROYAL INFIRMARY, GLASGOW

*With illustrations on plate*

IN this sporting age the more common forms of injury to which athletes are liable have been well documented (*The Practitioner* 1950); and their diagnosis and treatment present few problems. But one form of injury which, although comparatively common, has been mentioned in the literature only within recent years is athlete's or footballer's ankle. It has been suggested that the exact nature of the injury was not fully appreciated before and that it had been treated as a form of chronic sprain. On the other hand, there may be an actual increase in its incidence because sport today is so highly competitive. Morris (1943) first described the condition, which he termed athlete's ankle, because it affected the ankles of 5 athletes, each an expert in some particular sport.

Bony outgrowths occur along the tibial margins, beneath the malleoli (especially the medial one), and on the dorsum of the neck of the astragalus, as a result of repeated minor strains of the capsular attachments of the ankle-joint, and repeated compression injuries of the bones against each other when the ankle is forcibly dorsiflexed and plantarflexed. The posterior processes of the astragalus may be broken off and form loose bodies in the joint (McDougall 1955) (fig. 1).

### Clinical Features and X-ray Changes

Although the bone changes may be present at an early stage, the athlete is usually symptom-free until he has played his game for a number of years; he then gets pain at the attachment of the joint capsule along the tibial margin and the neck of the astragalus.

Footballers usually feel pain at the moment of impact with the ball, and by the end of a game the whole ankle feels sore. In a simple sprain the patient points to a localised tender area, but here he is less definite and indicates that the ankle-joint generally is painful. Tenderness is elicited on pressure along the capsular attachments and deep to the tendo achillis if the posterior aspect of the joint is affected. After several recurrences an effusion distends the ankle-joint, and is most apparent on either side of the extensor tendons.

Radiographic examination is diagnostic. The earliest change is peaking of the tibial margins (fig. 2), but later on definite bony overgrowth occurs along the tibial margins and on the neck of the astragalus (fig. 1). In a footballer, if the strain of kicking is partly borne by the mid-tarsal joint, the superior aspect of the navicular is drawn out into a sharp peak or broken off (figs. 3 and 4).

McMurray (1950) suggested the name "footballer's ankle" in the belief that the injury was peculiar to professional footballers, especially those over twenty-five who had played the game for several years. He believed that it did not occur in rugby players because the strain of kicking a rugby ball did not fall so directly on the ankle-joint, as happens with a soccer player, especially when the ball is "dead."

Association football is without doubt the most popular game in Great Britain, and its popularity has spread throughout the world; so it is not surprising that most patients suffering from this injury are footballers. But the injury is no respecter of age or status, and it is found after other forms of athletic activity. The age at which it appears depends on the enthusiasm with which the sport is undertaken, the degree of trauma to the ankles, and the weight of the player.

We have treated many amateur footballers, including a schoolboy international aged eighteen, and have noted the joint changes in rugby players, though to a less degree, because in this game the ball is not kicked so frequently.

One of the most striking examples was seen in a circus artist who had to hang suspended from a ladder by his feet, and who finally somersaulted from the ladder to the ground below, a distance of twenty feet (fig. 5). Numerous loose bodies were present in both anterior and posterior aspects of the joints, and there was considerable new bone formation. Despite these changes, he had continued with his performance until the day on which the radiographs were taken.

### Joint Changes

McMurray (1950) considered that the joint changes are not due to osteo-arthritis, for there is no involvement of the articular surfaces and the bony outgrowths lie above the articular margin. At operation, however, close inspection will reveal fibrillation of the articular cartilage at the joint margins; the area involved is not great, being limited to that part where the bones come into contact on movement. The bony outgrowths are actually within the capsule or in its deeper aspect; this was noted by McMurray in his first case.

Discussing the bony ridge which forms on the under aspect of the femoral neck in osteo-arthritis, Lloyd-Roberts (1953) suggests that it is due to the deposition of new bone within a subperiosteal space produced by traction, transmitted through the fibrotic capsule of the joint. This mechanism seems a likely one in the ankle-joint changes. Moreover, the bony changes can limit considerably the movements of the joint (fig. 3). My colleagues and I believe that this is a form of traumatic

arthritis of the ankle-joint, in which the changes are limited to the articular margins only because of the nature of the trauma.

In any first-class football team the ankle-joints of practically every player will show varying degrees of these changes; the bony outgrowths will be more definite in the backs who must kick the ball long distances with great force. Despite these changes most players finish their careers free from ankle trouble, unless the joint is subjected to a more severe injury than usual, which serves to determine the onset of symptoms. If a radiograph is taken at the time, small areas of ossification in the ligaments attract attention and the player is said to be suffering from a chipped ankle bone.

### Treatment

Thorndike (1950) states that it is possible by means of a modified figure-of-eight bandage to prevent joint-ligament sprains in all sports that require sudden twisting or pivoting. In these cases we advise such a bandage, or strapping, which undoubtedly supports the joint and diminishes the number of sprains. To be completely effective the bandage would have to be applied so as to interfere substantially with the function of the joint, and this is not practical.

When a player first complains of pain in the ankle, conservative treatment should be given a trial; McMurray (1950) found it ineffective, but with it a number of injuries settle down, and such a trial is justified.

The symptoms subside when the patient stops playing, so a period away from the game is advised. If the ankle is swollen a plaster cast is applied for three to four weeks. This is followed by four weeks' physiotherapy and ankle exercises; if at the end of this time the joint is free from pain when it is moved passively through its full range, training begins and is graduated until the player has returned to the field. If this conservative régime fails operation must be considered. As I have said, symptoms disappear once the athlete gives up his sport and we have found no evidence of any further deterioration thereafter. Operation is therefore only undertaken to enable a player to continue at his sport and such being the case is only advised when the individual is anxious to continue or stands to lose financially if he is unable to do so.

At operation after opening the capsule of the joint, the bony outgrowth is removed together with any loose bony ossicles. The bony outgrowth in the posterior aspect of the joint is never so large as to require removal, but any loose bony fragments should be dealt with because they may give rise to pain in the back of the joint.

A plaster cast is applied for four weeks after operation and this is followed by a period of physiotherapy and graduated exercises. Training is resumed at about the sixth week and the player should be fit to play in eight to ten weeks from the date of the operation.

During the past five and a half years, 29 players with this lesion have been treated. Of these, 17 had conservative treatment only; 12 were able to return to football, and 2 to rugby; but 3 continued to have pain, and as their football was only a pastime they gave it up. 12 players were operated on, 7 immediately because of the acuteness of symptoms and size of the outgrowths and 5 after failure of conservative treatment. Of these, 11 have returned to football; the twelfth continued to have discomfort, and as he was thirty-one years of age he decided to retire.

### Summary

A study of the condition known as athlete's or footballer's ankle indicates that the changes are a traumatic arthritis affecting only the marginal areas of the joint.

Conservative treatment is successful provided the changes are not excessive; in that case, operation is required.

Once a player gives up the game, the prognosis in this injury is excellent and no further deterioration occurs.

I wish to thank Mr. J. Patrick, who was in charge of these patients.

### REFERENCES

Lloyd-Roberts, G. C. (1953) *J. Bone Jt Surg.* **35B**, 627.
McDougall, A. (1955) *Ibid*, **37B**, 257.
McMurray, T. P. (1950) *Ibid*, **32B**, 68.
Morris, L. H. (1943) *Ibid*, **25**, 220.
*The Practitioner* (1950) **164**, 289.
Thorndike, A. (1950) *Practitioner*, **164**, 306.

## EARLY DIAGNOSIS OF COMPRESSION OF THE SPINAL CORD BY NEOPLASMS

G. F. ROWBOTHAM
B.Sc. Manc., F.R.C.S.
REGIONAL CONSULTANT IN NEUROLOGICAL SURGERY, GENERAL HOSPITAL, NEWCASTLE UPON TYNE

EXPERIENCE has shown that the early diagnosis of compression of the spinal cord, particularly by benign neoplasms such as meningiomata and neuromata, is one of the most difficult problems which confront a clinician. The classical syndromes are far too often those of the late stages of neural compression, when irreversible damage has already taken place.

Between 1941 and 1948, 80 cases of compression of the spinal cord by neoplasms came under my care (table I).

TABLE I—CASES OF COMPRESSION OF THE SPINAL CORD BY NEOPLASMS 1941–48

| — | Male | Female | Total |
|---|---|---|---|
| Primary neoplasms .. .. | 29 | 31 | 60 |
| Secondary neoplasms .. | 14 | 6 | 20 |
| | 43 | 37 | 80 |

I have analysed this group of cases to determine whether early diagnosis is possible without subjecting every patient suspected of spinal-cord compression to the dangers and discomforts of special investigations.

### Primary Neoplasms

EXTRAMEDULLARY PRIMARY NEOPLASMS

In this series of 80 cases there were 46 extramedullary neoplasms arising from one of the tissues of the spinal cord (table II). Theoretically it should have been possible to excise the 36 meningiomata and neuromata without inflicting permanent damage on the spinal cord, but unfortunately many of these patients were referred only when serious damage had already occurred.

Although complete removal of the neoplasm was possible in 36 cases, only 16 patients regained complete function of limbs, bladder, and rectum.

Of the remaining patients 13, although able to carry on useful lives, were left with some locomotor or sphinc-

TABLE II—PRIMARY NEOPLASMS OF THE SPINAL CORD

| | | | |
|---|---|---|---|
| ARISING FROM THE TISSUES OF THE SPINAL CORD: | | | |
| (a) *Extramedullary:* | | | |
| Meningiomata .. .. .. .. .. | 14 | | |
| Neuromata .. .. .. .. .. | 22 | | |
| Angiomata .. .. .. .. .. | 5 | | |
| Tumours of cauda equina: | | | |
| Giant-cell .. .. .. | 2 | | |
| Ependymoma .. .. .. | 2 | | |
| Embryoma .. .. .. | 1 | | |
| | | 5 | |
| | | | 46 |
| (b) *Intramedullary:* | | | |
| Gliomata .. .. .. .. .. | | | 6 |
| ARISING FROM THE SPINAL COLUMN: | | | |
| Osteoclastomata .. .. .. .. | 3 | | |
| Osteochondroma .. .. .. .. | 1 | | |
| Chondrosarcomata .. .. .. .. | 3 | | |
| | | | 7 |
| ARISING IN THE EXTRADURAL SPACE: | | | |
| Lymphosarcoma .. .. .. .. | | | 1 |
| | | | 60 |

teric disability, 3 were left with poor functional results, and 3 died from infections after operation. 1 patient was not operated on, because of deep and extensive bedsores.

*Meningiomata and Neuromata*

These 2 neoplasms are grouped together because, in their early stages, they present the same diagnostic and operative problems. Both types of tumour are essentially benign. In this group of cases 4 were situated in the cervical, 24 in the thoracic, and 8 in the lumbar area.

In 20 cases, the first symptom was severe pain of obvious segmental or posterior-root distribution, and in 12 the pain was situated deeply in or near the midline. When the pain was non-segmental there was rigidity of the spine and restriction of movement, and often tenderness on deep palpation. Pain was always severe.

Sensory change in a segmental distribution is an important early sign in posterior-root compression, and it is misleading to look for complete loss. When pain was the first symptom, it began many months before limb weakness. Unfortunately, it is in these signless months that a doctor may decide that there is nothing seriously wrong with his patient, or be tempted to defer further examination until too late. Should a root pain or central back pain be followed many months later by weakness of a limb, the possibility of spinal-cord compression should be fully investigated, and patients should never be allowed to become bedridden before special diagnostic tests have been carried out.

By the time paralysis is first noticed, lumbar puncture will almost certainly show an increase in the proteins of the cerebrospinal fluid (C.S.F.). It is not necessary for the proteins to have risen to 100 mg. per 100 ml. to make a diagnosis; given that the normal protein content is 40 mg. per 100 ml., a rise to 60 mg. should not be overlooked if there is the slightest suggestion of weakness of the legs. In this present group the figure was over 150 mg. per 100 ml. in all cases.

Absence of blockage of the C.S.F. pathways (negative Queckenstedt test) by no means excludes spinal compression. If there is the slightest suspicion of this, lumbar puncture and Queckenstedt tests should be repeated after four weeks, or sooner if the patient's paralysis becomes worse.

To wait for clear radiographic evidence of bony change is usually to wait too long. Should a lumbar puncture or Queckenstedt test become positive, or should paralysis advance rapidly, detailed myelographic examination is essential.

*Differential diagnosis.*—In 4 cases of this group the first symptom was weakness of the legs, unassociated with pain, or with sensory or sphincteric disturbance. Indeed, the diagnosis of disseminated sclerosis was made and sustained by clinicians for periods as long as eighteen months. In all of these cases operation proved the neoplasms to be anteriorly placed in the midline, so that the spinal cord was kinked over the swelling; the late appearance of sensory disturbances can therefore be explained anatomically. Even when the neoplasm was posteriorly placed, sensory changes referable to the long tracts were often late in appearing.

The C.S.F. proteins increase early in anteriorly placed neoplasms. In disseminated sclerosis the early changes are in the Lange curve, and not in the protein content. The prodromal signs and symptoms of disseminated sclerosis have been described by McAlpine (1955); but when there is the slightest doubt about the diagnosis repeated lumbar punctures and protein estimations are necessary.

In cases of progressive paralysis unassociated with other signs, the possibility of a parasaggital meningioma must be considered. When such a tumour is present radiographs of the skull will show enostosis, or enlargement or multiplication of the diploic channels and meningeal grooves. A parasaggital meningioma can cause considerable paraplegia without any accompanying signs or symptoms.

*Angiomata*

Angiomata of the spinal cord are often clinically indistinguishable from meningiomata and neuromata. In angiomata the cord may be considerably damaged without any rise in the C.S.F. proteins and without any blocks in the arachnoidal pathways, whereas in meningiomata or neuromata severe compression of the cord is nearly always associated with a positive Queckenstedt test and a raised level of C.S.F. protein. Angiomata elsewhere in the body may point to the correct diagnosis.

Straight radiography rarely shows angiomatous changes in the vertebral bodies, and there were negative findings in each of the 5 cases in this series.

Surgery has little to offer in the treatment of these neoplasms.

*Tumours of the Cauda Equina*

Almost all the benign tumours at this site give the same clinical picture.

Since the lumbar-puncture needle may be introduced above the block, protein values are apt to be low, and a Queckenstedt test may give misleading results. Sciatic pain, followed by sphincteric disturbance, weakness, and sensory loss in the perineum are indications for myelography.

In 2 of the 5 cases in this series, the lumbar-puncture needle was introduced into the tumour itself and blood was withdrawn; in each case this was dismissed as a "lumbar-puncture failure." This pitfall should always be kept in mind when a giant-cell tumour of the cauda equina is suspected clinically.

Spina bifida, associated with progressive spinal-cord compression at the corresponding level, should always suggest an underlying embryoma. Such cases were excluded from this series on radiographic evidence. Many tumours of the cauda equina can be successfully removed (as in 3 of the 5 cases in this series) in the early stages of the disease.

INTRAMEDULLARY PRIMARY NEOPLASMS

The clinical picture here is indistinguishable from that of syringomyelia. In this small group of 6 cases, the common first symptom was a "peculiar feeling somewhere in the body" which later developed into sensory loss of the dissociated type. Lower-motor-neurone paralysis and wasting of the muscles in the corresponding segments followed the sensory changes. Although the onset of paraplegia was late, its progress was rapid. Chemical changes in the C.S.F. and spinal blocks were also late developments. Surgery was of no value in these cases.

PRIMARY NEOPLASMS ARISING FROM THE SPINAL COLUMN

In this group there were 3 osteoclastomata, 1 osteochondroma, and 3 chondrosarcomata. The first symptom in each case was severe, persistent pain in the back, and in every instance there was clear radiographic evidence of pathological changes in the vertebræ before paralysis became advanced. Early diagnosis in these cases is made by radiography. Operation and decompression should be carried out at the first sign of spinal-cord compression, if the neoplasm is thought not to be highly malignant. A satisfactory result was obtained with 1 osteoclastoma in my group.

**Secondary Neoplasms**

In the 20 cases of compression of the spinal cord by secondary deposits the primary growths were situated as follows: bronchus, 7; prostate, 6; breast, 5; kidney, 1; and stomach, 1.

In 18 cases the nature of the lesion was known before the spinal cord became affected. In 12, bony deposits or erosion were revealed by radiography, and in 4, although there was no bony change, cancer was known to be present somewhere in the body. In the remaining

2 cases, it was impossible to establish the nature of the lesion before laminectomy. In these cases, biopsy established that the growths were of prostatic and renal origin. In the prostatic case the first symptom was a deep, boring pain between the shoulder-blades; and in the renal case it was non-segmental pain on the left side of the body, with weakness of the legs.

Root pain is commonly the first symptom of a neoplasm arising in the posterior abdominal or thoracic wall. The growth tends to enter the spinal canal through the intervertebral foramina and wrap itself round the spinal theca, not only crushing the cord, but also strangling its foraminal blood-supply. Ischæmia as much as constriction of the cord accounts for the neural changes, and this explains why decompression and removal of the growth so rarely relieves the symptoms. The purpose of operation is usually to relieve pain.

### Discussion

In malignant constriction of the spinal cord by a silent primary neoplasm the neurological signs are much the same as those caused by the compression of a primary benign neoplasm. But in cancerous cases the patient may be fully paralysed within a few days of the first signs of weakness; whereas in cases of benign neoplasm the paralysis develops slowly over months or even years.

It is impossible to identify the origin of spinal-cord compression by the first symptom. A persistent pain of root distribution suggests a physical origin, and aggravation by straining or coughing confirms this.

At the other end of the scale is the picture of complete paralysis, of gross sensory loss, of sphincteric paralysis, of decubitus ulcers, and of ascending infection of the kidneys.

A diagnosis should be made as soon as possible after the appearance of the first symptom. Neoplasms that are surgically curable nearly always progress slowly, and it is often possible to make a diagnosis on clinical evidence alone before irreversible damage has been done to the spinal cord.

I thank Dr. Raymond Whitehead, of the department of pathology of Manchester University, for his helpful criticisms. The preparation of this work was assisted by a research grant from No. 1 Regional Hospital Board.

REFERENCE

McAlpine, D. (1955) *Lancet*, *i*, 1033.

## THE NON-ANTIGENICITY OF CHONDROITIN SULPHATE

W. C. BOAKE
B.Sc., M.B. Melb., M.R.C.P.
ASSISTANT, MEDICAL UNIT

H. MUIR
M.A., D.Phil. Oxfd
EMPIRE RHEUMATISM COUNCIL FELLOW

ST. MARY'S HOSPITAL, LONDON

IT has often been suggested that rheumatic fever and acute glomerulonephritis are due to the fact that the patient's tissues have become antigenic. This concept has been largely based on the undoubted association between these diseases and antecedent β-hæmolytic streptococcal infection. It is thought that these streptococci react with a normally non-antigenic component of the host's tissues (generally assumed to be a connective-tissue component in rheumatism), rendering it antigenic. The auto-antibodies thus formed are thought to react in situ with the changed or unchanged body component and so to produce the characteristic local lesions.

This hypothesis has never definitely been proved or disproved, although it has been the subject of much experimental work:

Cavelti and Cavelti (1945) produced glomerulonephritis in rats by repeated injection of dead streptococci together with rat-kidney tissue. At the same time, antibodies were formed against the rat kidney. This work, however, has not been confirmed (Humphrey 1948).

McKee and Swineford (1951) injected guineapigs with a vaccine made from dead hæmolytic streptococci and guinea-pig-joint tissue. No joint or kidney lesions or precipitins were found.

Glynn and Holborow (1952a) produced arthritis in rabbits by a somewhat similar technique. They injected rabbits with a vaccine prepared from β-hæmolytic streptococci and chondroitin sulphate, a polysaccharide derived from human cartilage. These rabbits developed swollen joints and synovitis. This work differed from similar studies, however, in that Glynn and Holborow prepared their vaccine by incubating chondroitin sulphate with live β-hæmolytic streptococci, because they had already shown that this process conferred antigenicity on normally non-antigenic polysaccharides of vegetable origin (Glynn and Holborow 1952b).

We thought that their technique might be valuable in work on rheumatism. We therefore repeated this work but, in doing so, used rabbit protein-free chondroitin sulphate and a larger number of rabbits. (Glynn and Holborow used only very few rabbits and prepared their vaccine from human chondroitin sulphate.) Although human and rabbit chondroitin sulphate may be identical, nothing is known about the immunological relations of these two substances. To demonstrate auto-antibody production it was clearly necessary to use a substance derived from an animal of the same species as that subjected to the experiment.

### Materials and Methods

The methods described by Glynn and Holborow (1952a) were followed closely, and their paper should be consulted.

*Potassium Chondroitin Sulphate*

Chondroitin sulphate was prepared by the method of Einbinder and Schubert (1950) from cartilage obtained from ears, trachea, and ribs of ten rabbits. Connective tissue and muscle were removed. The cartilage was sliced and suspended in a solution containing 30% potassium chloride and 1% potassium carbonate, and macerated in a Waring blender. It was twice extracted for forty-eight hours with this solution. The product obtained was purified twice more by the method of Einbinder and Schubert (1950) and dried in vacuo over phosphorus pentoxide.

The resultant product contained hexosamine [1] 30·7%, nitrogen [2] 2·15%, and potassium 13·6%. The formula for chondroitin being $C_{14}H_{19}O_{14}NSK_2 2H_2O$, one would expect to find hexosamine 31·5%, nitrogen 2·45%, and potassium 13·66%. Einbinder and Schubert (1950) found in their potassium chondroitin sulphate from ox trachea hexosamine 22·43–26·36%, nitrogen 2·07–2·18%, and potassium 10·95–11·3%. The low nitrogen content of the preparation and the fact that it gave a negative Biuret reaction suggest that it contained little, if any, protein.

For use in the experiment the chondroitin sulphate was dissolved in sterile water in a concentration of 10 mg. per ml. (1% *w/v*). This was sterilised by Seitz filtration, which led to a loss of 30% of the material, determined by nitrogen estimations on the filtrate. The sterile solution was therefore considered to contain 0·7% *w/v* of chondroitin sulphate.

*Preparation of Vaccines*

A group-A type-4 strain of a β-hæmolytic streptococcus was obtained from the National Collection of Type Cultures and cultured for eighteen hours in tryptic-digest broth, centrifuged, washed twice with physio-

1. Determined by a modification of the method of Elson and Morgan (1933)
2. Determined by the method of Conway (1947).

logical saline solution, and resuspended in a concentration of $10^9$ per ml. The live streptococci were then incubated with an equal volume of a 0·7% *w/v* sterile solution of chondroitin sulphate for an hour at 37°C, centrifuged again, washed twice, resuspended in physiological saline solution in a concentration of $10^9$ per ml., and killed by heating to 56°C for 30 minutes. Control vaccines were prepared in the same way but without the chondroitin sulphate.

*Immunisation*

Young cross-bred rabbits weighing 2·0–2·8 kg. were kept on a mixed diet in individual cages. Twelve selected at random were given intravenous injections of chondroitin-sulphate vaccine three times a week. Seven injections were given initially, the dosage per injection being 0·1, 0·2, 0·2, 0·5, 0·5, 1·0, and 1·0 ml. (total 3·5 ml.). A booster dose of 1·0 ml. was given two weeks after the first course of injections. The vaccine was always freshly prepared for each injection.

Six other rabbits were injected intravenously with heat-killed chondroitin-free streptococci in the same dosage as stated above. Six other rabbits received only chondroitin-sulphate solution 3 mg. per rabbit.

*Tests for Antibodies to Chondroitin Sulphate*

*Pricipitins.*—The method of Swift et al. (1943), as used by Glynn and Holborow (1952a) was followed exactly, except that all the sera were tested in dilutions of 1/1, 1/10, 1/20, and so on, to 1/1280.

*Complement fixation.*—The method of Wyler (1929), as used by Ackroyd (1951), was adopted. Sera were diluted 1/1, 1/2, 1/3, 1/4 . . . 1/10, 1/15, 1/20. These tests were made on all sera obtained later than three weeks after the start of the experiment.

*Skin sensitivity* to chondroitin sulphate was tested by injecting intradermally in the flank 0·1 ml. of a 0·7% *w/v* solution of chondroitin sulphate. The skin was examined twenty-four and forty-eight hours after the injection.

## Results

*Clinical Manifestations of Arthritis*

No rabbit in any of the three groups at any time before, during, or up to a month after the last injection had swollen, stiff, or tender joints. All had persistently normal gaits, and all gained weight throughout the experiment. Three control rabbits died; two from respiratory infections, and one from intestinal obstruction.

*Pathological Manifestations of Arthritis*

Ten rabbits given chondroitin-sulphate vaccine were killed a month after the last injection. Their pericardial, pleural, and peritoneal membranes were all normal. Their hip, knee, shoulder, elbow, and temporomandibular joints were all macroscopically normal. Synovial membrane from at least one joint from each rabbit was examined microscopically and found to be normal. None of the control rabbits showed any abnormality of the joints.

*Antigenicity of Rabbit Chondroitin Sulphate*

No precipitins or complement-fixing antibodies to chondroitin sulphate were found in any of the sera of any of the rabbits at any time. Streptococcal agglutinins developed in all the rabbits injected with streptococci.

*Skin-sensitivity to Rabbit Chondroitin Sulphate*

No rabbit at any time developed skin sensitivity to chondroitin sulphate.

## Discussion

The failure to find auto-antibodies to rabbit chondroitin sulphate and to produce experimental arthritis is of some interest. The only apparent difference between this experiment and that of Glynn and Holborow (1952a) was in the chondroitin sulphate used. It is also possible, however, that in this work there was no definite combination between the rabbit chondroitin sulphate and the streptococci. We have no formal proof that this union took place; if it did not, this is a possible explanation of our negative results.

On the other hand, the results obtained by Glynn and Holborow (1952a) may not have been due to chondroitin sulphate acting as an auto-antigen but could possibly be interpreted as a sensitisation reaction to traces of protein in the chondroitin preparation.

In any case, our findings show once again that positive results obtained by techniques involving auto-antibody production are difficult to repeat. Such methods are not yet reliable and add little to current concepts on the ætiology of rheumatism. Burnet (1954) points out that "until a well-defined circulating antibody of the type postulated can be demonstrated in every case of rheumatic fever at the appropriate period" ideas must remain speculative.

Although these experimental results were also negative, we have thought it worth while to record them because they were obtained under well-defined conditions.

## Summary

An attempt was made to produce auto-antibodies and arthritis in rabbits by injecting a vaccine consisting of rabbit chondroitin sulphate and hæmolytic streptococci.

No auto-antibodies were detected, and no rabbit developed arthritis.

We wish to thank Prof. G. W. Pickering and Dr. J. F. Ackroyd for their criticism, and Mr. D. Pullen for his technical assistance. One of us (W. C. B.) was in receipt of a research grant from the endowment fund of St. Mary's Hospital.

### REFERENCES

Ackroyd, J. F. (1951) *Clin. Sci.* **10**, 185.
Burnet, M. (1954) *Brit. med. J.* ii, 189.
Cavelti, P. A., Cavelti, E. S. (1945) *Arch. Path.* **39**, 148; **40**, 158, 163.
Conway, E. J. (1947) Microdiffusion Analysis and Volumetric Error. 2nd ed., London.
Einbinder, J., Schubert, M. (1950) *J. biol. Chem.* **185**, 725.
Elson, L. A., Morgan, W. T. J. (1933) *Biochem. J.* **27**, 1824.
Glynn, L. E., Holborow, E. J. (1952a) *Lancet*, ii, 449.
— — (1952b) *J. Path. Bact.* **64**, 775.
Humphrey, J. H. (1948) *Ibid*, **60**, 211.
McKee, K. T., Swineford, O. jun. (1951) *Ann. rheum. Dis.* **10**, 116.
Swift, H. F., Wilson, A. T., Lancefield, R. C. (1943) *J. exp. Med.* **78**, 127.
Wyler, E. J. (1929) *Spec. Rep. Ser. med. Res. Coun., Lond.* no. 129.

# OUTPATIENT TRIAL OF ACETAZOLEAMIDE IN PREVENTION OF PRE-ECLAMPTIC TOXÆMIA

H. SCHNIEDEN *
M.D. Bristol
BEAVERBROOK RESEARCH FELLOW

*From the Departments of Obstetrics and Gynæcology and of Pharmacology, University of Bristol*

THERE is evidence that sodium retention may develop in pre-eclamptic toxæmia. Dieckmann et al. (1952a) reported on the inability of patients with pre-eclamptic toxæmia to excrete a sodium load in a similar manner to healthy pregnant women. Carey (1953) found an increased sodium space in patients with mild pre-eclamptic symptoms, and Chart et al. (1951) noted increased excretion of sodium-retaining factors in the urine of such patients. In an attempt to prevent sodium retention low-sodium diets have been given, but it is difficult to reduce the sodium content of the diet below 1 g. daily without rendering the diet unpalatable.

Ion-exchange resins (Odell et al. 1951, Carey 1952, Dunster 1953) have been given in conjunction with a low-sodium diet to prevent absorption of sodium from the

* Present address: Department of Physiology, University College, Ibadan, Nigeria.

gastro-intestinal tract, but the large quantity of ion-exchange resin that has to be given daily is bulky and unpalatable, and other ions are adsorbed. It therefore seemed of interest to see whether acetazoleamide, which increases sodium excretion by inhibiting the carbonic anhydrase in the kidneys, would be of use in preventing pre-eclamptic toxæmia.

## Methods

Patients who had gained more than 6 lb. in weight in any month after the 20th week of their pregnancy but had no other signs of pre-eclamptic toxæmia were referred to a special clinic, where they received one of the following treatments:

(1) A low-sodium diet plus acetazoleamide.
(2) A moderately low-sodium diet plus acetazoleamide.
(3) A low sodium diet plus a placebo.
(4) A moderately low-sodium diet plus a placebo.

The diet provided 1800 calories daily and contained 175 g. of carbohydrate, 96 g. of protein, and 70 g. of fat. The low-sodium diet provided 1·2 g. of sodium ($Na^+$) and the moderately low-sodium diet 3·0 g. of sodium daily.

To eliminate bias the treatments given were decided before the patients were examined. The first patient arriving at the special clinic received treatment 1, the second treatment 2, and so on. Each patient on arrival was given a code number so that the investigator at the subsequent examination did not know what treatment was being given.

TABLE I—NUMBER OF PATIENTS WHO DEVELOPED PRE-ECLAMPTIC TOXÆMIA

| Diet | Treatment | Primiparæ | Multiparæ |
|---|---|---|---|
| Low-sodium | Acetazoleamide | 2 of 13 | 1 of 13 |
| | Placebo | 8 of 11 | 7 of 13 |
| Moderately low-sodium | Acetazoleamide | 5 of 14 | 1 of 8 |
| Moderately low-sodium | Placebo | 5 of 12 | 4 of 9 |

All the patients showed an increase of weight of more than 6 lb. a month before treatment.
$\chi^2$ test $P > 0{\cdot}01 < 0{\cdot}02$ for both primiparæ and multiparæ (low-sodium diet).
$\chi^2$ test $P > 0{\cdot}5 < 0{\cdot}7$ for primiparæ (moderately low-sodium diet), and $P > 0{\cdot}1 < 0{\cdot}2$ for multiparæ.

The patients were seen once a month in the earlier stages of their pregnancy and weekly in the final month. They were considered to have developed pre-eclamptic toxæmia if they showed any one of the following signs: clinical œdema of both hands and legs; a diastolic blood-pressure above 90 mm. Hg; and albuminuria. The blood-pressure and clinical œdema were assessed by the same observers throughout the series. Blood-pressure was measured by an experienced sister and checked by a doctor. Good correlation was obtained. Visible œdema was judged by a doctor. Acetazoleamide was given orally in a dose of 250 mg. every third day. Urinary sodium was estimated with an internal standard flame-photometer.

## Results

The number of cases which developed signs of pre-eclamptic toxæmia is shown in table I. Acetazoleamide significantly decreased the incidence of signs of pre-eclamptic toxæmia in the patients on the low-sodium diet whether they were primiparæ or multiparæ ($\chi^2$ test P between 0·01 and 0·02 for primiparæ and multiparæ). In primiparæ on the moderately high-sodium diet acetazoleamide produced no significant difference. The numbers of multiparæ investigated on this diet were too few to prove that it had no effect. The number of patients who developed albuminuria, visible œdema of both legs and hands, or a diastolic pressure greater than 90 mm. Hg during the period of observation is shown in table II. The mean weekly gain in weight in all groups treated with acetazoleamide was less than that of controls, but the differences were not significant. The onset of œdema was often not associated with a sudden increase in the patient's weight.

TABLE II—NUMBER OF PATIENTS WHO DEVELOPED ALBUMINURIA, VISIBLE ŒDEMA, OR A DIASTOLIC BLOOD-PRESSURE HIGHER THAN 90 MM. HG DURING PERIOD OF OBSERVATION

| Treatment | Primiparæ | | | Multiparæ | | |
|---|---|---|---|---|---|---|
| | No. of patients | Diastolic blood-pressure > 90 mm. Hg | Visible œdema | No. of patients | Diastolic blood-pressure > 90 mm. Hg | Visible œdema |
| Low-sodium diet plus acetazoleamide | 13 | 0 | 2 | 13 | 0 | 1 |
| Low-sodium diet plus placebo | 11 | 2 | 6 | 13 | 4 | 3† |
| Moderately low-sodium diet plus acetazoleamide | 14 | 4* | 1 | 8 | 0 | 1 |
| Moderately low-sodium diet plus placebo | 12 | 2 | 3 | 9 | 0 | 4 |

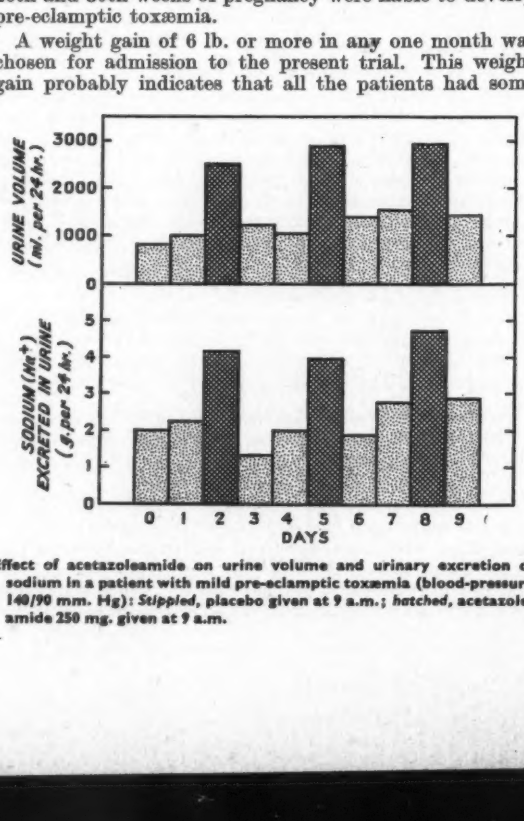
* One patient also had albuminuria.
† One patient also had a diastolic blood-pressure > 90 mm. Hg.

It was impossible to estimate the urinary excretion of sodium in outpatients treated with acetazoleamide, but it was estimated in three inpatients with established pre-eclamptic toxæmia. Acetazoleamide repeatedly produced a sodium diuresis in one of these patients (see figure); each diuresis lasted about twenty-four hours. In the two other inpatients with pre-eclamptic toxæmia no sodium diuresis was obtained.

## Discussion

Cummings (1934) found that the average monthly gain in weight in the last few months of pregnancy ranged from 3 lb. in the 8th and 9th months to 5 lb. in the 6th and 7th months, and Evans (1937) noted that 47% of expectant mothers who had a weight gain of 6–8 lb. in any month of their pregnancy developed toxæmia. Dieckmann et al. (1952b) reported that the normal weight gain between the 20th and 30th weeks of pregnancy was 7·7 lb., and Hamlin (1952, 1953) considered that patients who gained more than 8 lb. between the 20th and 30th weeks of pregnancy were liable to develop pre-eclamptic toxæmia.

A weight gain of 6 lb. or more in any one month was chosen for admission to the present trial. This weight gain probably indicates that all the patients had some




**Effect of acetazoleamide on urine volume and urinary excretion of sodium in a patient with mild pre-eclamptic toxæmia (blood-pressure 140/90 mm. Hg): *Stippled*, placebo given at 9 a.m.; *hatched*, acetazoleamide 250 mg. given at 9 a.m.**

degree of water retention on admission to the trial. The onset of visible œdema without further sudden increase in body-weight may be due to shift of fluid from the intracellular to extracellular spaces. Dieckmann (1952) states that clinical œdema is usually due to an increased extracellular fluid space, but that fluid retention may be primarily intracellular.

The standards of blood-pressure in normal pregnancy set by various workers varies considerably. DeLee and Greenhill (1948) took 130/90 mm. Hg as the highest limit of normality. Brews (1948), however, considered that 140/90 mm. Hg had to be recorded before a patient could be considered to have pre-eclamptic toxæmia. Browne and Browne (1955) believed that a blood-pressure of 120/80 mm. Hg was pathognomonic.

In the present series the diastolic pressure alone has been considered, because Mukherjee and Govan (1950) and Hughes (1951) consider that a rise of diastolic pressure to be more significant than that of systolic pressure. The present results suggest (table II) that acetazoleamide may prevent a rise in diastolic blood-pressure. Possibly its effect on sodium metabolism may be responsible for this. Restriction of sodium is well known to have a beneficial effect on essential hypertension.

Diuretics have been used previously in the treatment of pre-eclamptic toxæmia. De Alvarez and Richards (1952) have reported that aminophylline and 'Mercuhydrin' induce a diuretic response in patients with pregnancy toxæmia. Assali et al. (1955), who investigated the effect of ammonium chloride, say "it appears that the inability of ammonium chloride to mobilise significant amounts of sodium limits its value in the treatment of the œdema of toxæmia of pregnancy." Acetazoleamide has been used in the treatment of œdema of congestive heart-failure (Friedberg and Halpern 1952, Gasch and Krück 1953, Belsky 1953, Falbriard 1954, Ruskin 1955). The doses used in those studies were 250–750 mg. daily. In the present investigation 250 mg. was given once every three days. This low dose had no untoward effect on the fœtus. Acetazoleamide was administered only every third day because resistance had been reported with daily doses (Hofbauer et al. 1955). Toxic manifestations were seen in two patients only: one complained of tingling in her hands, and another of nausea and epigastric pain. These symptoms ceased when acetazoleamide was withheld.

One would not be surprised to find that acetazoleamide fails in some patients with pre-eclamptic toxæmia. In severe congestive heart-failure Evans et al. (1954) have reported its failure to increase the urinary excretion of sodium. The main action of acetazoleamide is on the renal tubule, but W. S. Braverman, A. L. Rubin, and A. W. Mead (personal communication) found that it also decreased the glomerular filtration-rate in healthy people, although Ruskin (1955) has reported that it had no significant effect on the glomerular filtration-rate in patients with heart-disease. In pre-eclamptic toxæmia De Alvarez and Richard (1954) have noted a decrease in glomerular filtration-rate. Therefore, if acetazoleamide further decreases the glomerular filtration-rate, its effect on the renal tubule may be nullified.

### Summary

A selected series of pregnant patients were placed on a low-sodium (1·2 g. of $Na^+$ daily) or moderately low-sodium diet (3·0 g. of $Na^+$ daily), and some were treated with acetazoleamide.

The incidence of signs of pre-eclamptic toxæmia was significantly lower in patients who received acetazoleamide in addition to the low-sodium diet, but no significant difference was found in patients who received acetazoleamide in addition to a moderately low-sodium diet.

Acetazoleamide may produce a sodium diuresis in established pre-eclamptic toxæmia.

I thank Prof. G. G. Lennon and Prof. H. Heller for their interest and criticisms; Dr. S. Walker for facilitating the outpatient trial; Sister E. M. Staton for invaluable assistance in the special clinic; and Miss E. H. L. Duncan for statistical assessment of the results. Dr. F. C. Ottati and Dr. A. T. Mennie of Lederle Laboratories Ltd. kindly supplied the acetazoleamide ('Diamox') and placebos.

### REFERENCES

Assali, N. S., Herzig, D., Singh, B. P. (1955) *J. appl. Physiol.* **7**, 367.
Belsky, H. (1953) *New Engl. J. Med.* **249**, 140.
Brews, A. (1948) Eden and Holland's Manual of Obstetrics. 9th ed., London.
Browne, F. J., Browne, J. C. M. (1955) Antenatal and Postnatal Care. London; chapter 3.
Carey, H. M. (1952) *J. Obstet. Gynæc., Brit. Emp.* **59**, 67.
— (1953) *Proc. R. Soc. Med.* **46**, 396.
Chart, J. J., Shipley, E. G., Gordon, E. S. (1951) *Proc. Soc. exp. Biol., N.Y.* **78**, 244.
Cummings, H. H. (1934) *Amer. J. Obstet. Gynec.* **27**, 808.
De Alvarez, R. R., Richards, D. F. (1952) *Ibid*, **63**, 1263.
— — (1954) *Ibid*, **68**, 159.
DeLee, J. B., Greenhill, J. P. (1948) Principles and Practice of Obstetrics. Philadelphia.
Dieckmann, W. J. (1952) The Toxæmias of Pregnancy. 2nd ed., London; p. 305.
— Pottinger, E. E., Rynkiewicz, L. M. (1952a) *Amer. J. Obstet. Gynec.* **63**, 783.
— Smitter, R. C., Rynkiewicz, L. (1952b) *Ibid*, **64**, 850.
Dunster, M. (1953) *Proc. R. Soc. Med.* **46**, 401.
Evans, B. M., Jones, N. C. H., Milne, M. D., Steiner, S. (1954) *Clin. Sci.* **13**, 305.
Evans, M. D. A. (1937) *Brit. med. J.* i, 157.
Falbriard, A. (1954) *Praxis*, **43**, 293.
Friedberg, C. K., Halpern, M. (1952) *Fed. Proc.* **11**, 49.
Gasch, J., Krück, F. (1953) *Klin. Wschr.* **31**, 285.
Hamlin, R. H. J. (1952) *Lancet*, i, 64.
— (1953) *Proc. R. Soc. Med.* **46**, 393.
Hofbauer, K., Kaindl, F., Reinhardt, F. (1955) *Wien. Z. inn. Med.* **36**, 93.
Hughes, T. D. (1951) *Med. J. Aust.* ii, 871.
Mukherjee, C. L., Govan, A. D. T. (1950) *J. Obstet. Gynec., Brit. Emp.* **57**, 941.
Odell, L. D., Janssen, G. A., Novelli, J. C., Ralston, D. G. (1951) *Amer. J. Obstet. Gynec.* **62**, 121.
Ruskin, A. (1955) *Arch. intern. Med.* **95**, 24.

## GASTRO-JEJUNO-COLIC FISTULA

JAMES A. RHIND
B.Sc., M.B. Leeds, F.R.C.S.
SURGEON, PONTEFRACT AND CASTLEFORD HOSPITALS GROUP

"Gastro-jejuno-colic fistula . . . results in incessant diarrhœa, true fæcal vomiting sometimes, and rapidly progressive cachexia and decline. Untreated patients die in a few days or a few months. Pain, almost invariable in uncomplicated jejunal ulcer, usually lessens and disappears after the fistula is established" (Aird 1950). Lowdon (1953), in a report on forty-six cases of fistula in the Edinburgh Royal Infirmary, recognised that mild cases occurred but thought these uncommon.

Five consecutive cases in the Pontefract General Infirmary have shown features differing widely from those commonly described.

### Case-reports

**Case 1.**—A man, aged 52, began having indigestion in 1930. His case-notes in February, 1938, record pain two hours after meals, in attacks lasting a few weeks, with intervals of freedom. Fractional test-meal showed normal acid secretion. It is assumed that medical treatment was prescribed and failed, for he returned in October, 1938, for operation. This revealed a duodenal ulcer, and posterior gastro-enterostomy was performed.

He attended my outpatient clinic in November, 1952, when he complained of "stomach trouble" ever since his operation. There were remissions of three months between the attacks, but he was absent from work for about three months every year. His chief symptoms were pain and vomiting, the vomit having a foul smell. Bowel action had been normal, except for an attack of diarrhœa, lasting three weeks, six months previously. He had lost no weight. A tentative diagnosis of gastro-jejuno-colic fistula was confirmed by barium enema; a barium meal did not show this fistula, or any abnormality except the gastrojejunostomy and a deformed duodenum.

He was admitted to hospital in November, 1952, and given succinylsulphathiazole and streptomycin by mouth for three days before operation. The gastrojejunostomy was found to

be puckered and contracted by active ulceration, and the diameter of the gastro-jejuno-colic fistula was 1/4 in. The anastomosis and fistula were separated and the holes closed by simple infolding; a high partial gastrectomy was then performed. This operation did not upset the patient unduly, and his recovery was uneventful. He was transferred to a convalescent hospital on the seventh postoperative day, and he went home on the fourteenth.

In this case the fistula was suspected from the previous history rather than from the patient's symptoms. Although the barium enema showed a fistula, and its presence was confirmed at operation, his symptoms were so slight that the fistula must be regarded as "latent." The operation was no more difficult than a partial gastrectomy for a gastric ulcer, and the risks were slight.

**Case 2.**—A man, aged 33, began having indigestion in 1946. He was investigated in 1951, when a duodenal ulcer was diagnosed radiographically. The presence of an ulcer was confirmed at operation on June 4, when a partial gastrectomy of the Hoffmeister type with a retrocolic anastomosis was performed. On July 24, 1951, he was readmitted to hospital, radiography having shown a gastrojejunal ulcer. He received medical treatment in hospital for four months; during this time his symptoms disappeared, and repeated radiographic examination showed no further evidence of an anastomotic ulcer.

His pain returned in April, 1952, when he had severe diarrhœa for two weeks; thereafter slight diarrhœa persisted for two months, with foul eructations and vomiting. He attended my outpatient clinic in November, 1952. His chief complaint was pain, mostly in the lower abdomen with radiation to the back, but also in the upper abdomen; the pain was sometimes relieved by milk and alkalis. He had no vomiting, and bowel action had been normal for four months. Fractional test-meal showed acid secretion a little above the normal, and a barium meal showed a large ulcer crater in the jejunum near the stoma. An insulin test-meal produced free acid rising to 130 ml. *N*/10 HCl.

On Nov. 27, 1952, transthoracic vagotomy was performed. This route was chosen to avoid adhesions in the upper abdomen. It was therefore a little disappointing to find the base of the lung adherent to the diaphragm, presumably owing to previous subphrenic inflammation. The operation did not upset the patient, and his pain was relieved. A week later an insulin test-meal produced no free acid. About this time he began having slight diarrhœa. This was at first ascribed to the vagotomy, but a barium enema showed a gastro-jejuno-colic fistula. He was advised to have a further operation, but refused and went home on Dec. 10.

He remained free from pain until Jan. 4, 1953. On the following day he was admitted to hospital with an obvious perforation. His abdomen was opened five hours after the onset of pain, and a large opening was seen in the anastomosis. A finger was passed easily through the perforation into the stomach, colon, and jejunum. The edges of the hole were so fibrosed that simple closure seemed useless, and the surrounding tissues were too rigid to infold. The colon was separated from the gastrojejunostomy with great difficulty, because of the indurated adhesions, and the openings were closed in two layers. The contamination of the peritoneum was not obviously fæcal, but paralytic ileus was anticipated. The patient's postoperative progress was, however, completely uneventful and he made a rapid recovery. When reviewed in June, 1955, he had had no further trouble, and was well and working.

A fistula was considered at the first interview, although symptoms of this had been absent for at least four months. A jejunal ulcer after gastrectomy is seldom recognised radiographically, and hyperchlorhydria is uncommon after a fairly extensive gastrectomy. These findings diverted attention from the possible fistula until the "vagotomy diarrhœa" started. At that time we had no reason to doubt the usual teaching, that a fistula encourages healing of ulceration; and since a vagotomy also reduces anastomotic ulceration, we wondered whether the fistula might eventually be closed by healing. When the patient refused further operation, we had the opportunity of testing this idea. That his ulcer might perforate was a possibility we had not considered. His general condition must have been good, because he survived the very difficult operation of repair of the fistula while he also had a perforation.

**Case 3.**—A man, aged 51, had an acute perforation of a duodenal ulcer in 1942, and posterior gastrojejunostomy was performed in 1947. Following this he was well for eighteen months, after which his dyspepsia recurred and radiography showed a jejunal ulcer. He was advised to consult a surgeon but did not do so.

He attended the outpatient clinic of my colleague, Mr. Denley Clark, in December, 1953. For twelve months he had had no pain but for the past five weeks he had had diarrhœa and vomiting, the vomit being very offensive; and he had lost a lot of weight. Fractional test-meal showed high acid secretion. Barium enema revealed a gastro-jejuno-colic fistula, which had not been shown by barium meal.

After preparation of the intestine with chloramphenicol, his abdomen was explored in January, 1954, by Mr. Denley Clark. The stomach was large and the duodenum stenosed, although there was no active duodenal ulceration. There was a large gastro-jejuno-colic fistula, but no active anastomotic ulcer. The fistula was separated and the openings closed. Three-quarters of the stomach was removed and gastroduodenostomy performed (Billroth-1 operation). This procedure did not upset the patient, and his convalescence was uneventful.

He was well until December, 1954, when he developed vague symptoms, including backache. "Influenza" was diagnosed, but after seven days, he had severe melæna and hæmatemesis, and he was admitted to a medical ward in a state of collapse. With rapid blood-transfusions he improved, but twelve hours later he again vomited a large amount of red blood, and again collapsed. He was given further rapid transfusion, and I operated on him.

On the posterior wall of the Billroth-1 anastomosis there was an ulcer 1 in. in diameter, eroding the pancreas. When a clot was removed, the gastroduodenal artery was seen spurting in the base of the ulcer. The outer layer of the anastomosis had been completed with silk, and a piece of this was hanging in the stomach. A little more of the stomach was removed, and continuity restored by gastrojejunostomy.

This patient was the only one who had symptoms of a fistula. Even so, his general condition before the operation for fistula did not cause alarm, and his preoperative preparation consisted only in lavage of the stomach and colon, and chemotherapy. The anastomotic ulcer after gastrectomy was sufficiently severe to penetrate the pancreas and erode the gastroduodenal artery.

**Case 4.**—A man, aged 50, had acute perforations of peptic ulcers in 1929 and 1935. Posterior gastro-enterostomy was performed in 1940 for a "pyloric gastric ulcer causing much stenosis." He then served in the Royal Air Force until a further perforation was repaired in 1944, when he was discharged.

His weight had risen from his normal 10 st. 2 lb. to 12 st. 4 lb. while he was in the R.A.F., but fell to 10 st. 9 lb. at the time of the perforation, and remained steady until his next operation. He frequently had diarrhœa after his first perforation; from 1952 onwards, although his bowels moved only once, or at the most twice, a day, the stool was always liquid. In August, 1954, he was admitted to a Ministry of Pensions hospital with severe pain and vomiting. The pain was most severe in the xiphisternal region, but spread all over the epigastrium and through to the right loin. Barium meal showed that the gastrojejunostomy stoma was not working well, and most of the barium passed through a deformed and tender duodenum. Fractional test-meal showed acid secretion above the normal. He was given medical treatment, including an intragastric milk drip, and later a barium meal showed that most of the barium passed through the gastrojejunostomy stoma, which appeared normal. When he went home on Oct. 30, after ten weeks' treatment, his pain had gone and his stools were solid. After a few days, however, his pain returned and his stools became liquid again.

He was admitted to hospital under my care on Nov. 21, 1954, with an obvious perforation. At operation typical contamination of the peritoneal cavity was found. Examination of the anastomosis showed the induration of an ulcer, which was easily felt through the colon; there was, however, no perforation there. The duodenum was exposed with difficulty because of old adhesions to the back of his operation

scars; a perforation was seen and closed. His recovery was uneventful.

After three day's preparation with succinylsulphathiazole and oral streptomycin, his abdomen was reopened on Dec. 8, and the presence of a gastro-jejuno-colic fistula was confirmed. The anastomosis and fistula were separated, and the holes closed and oversewn. Partial gastrectomy was then performed, the duodenum presenting some difficulty because of the continued activity of the ulcer. The patient's post-operative progress was uneventful, and he went home on Dec. 22. He attended in June, 1955, when he had returned to work. The usual "small stomach" symptoms were improving, but he had lost a stone in weight. His stools were consistently solid for the first time in twenty years.

This patient's duodenal ulcer was active in the presence of a gastro-enterostomy and gastro-jejuno-colic fistula. His bowel history is difficult to interpret, because his liquid stools dated from the first perforation; probably the consistently liquid stools for two years signified that the fistula was open, and this was confirmed by the presence of solid stools after closure of the fistula. His duodenal ulcer perforated despite a recent long course of medical treatment. His loss of weight since gastrectomy shows that his fistula had not reduced him to "skin and bones."

**Case 5.**—A man, aged 57, began having indigestion in 1925. His abdomen was opened in 1928 for an acute perforation of a duodenal ulcer. The perforation was closed and a posterior gastro-enterostomy performed; his appendix was also removed. He had had indigestion ever since then, with gradually increasing pain. I was called to see him at home in April, 1955, when the pain was severe enough to make him stay in bed. His pain was felt in the epigastrium and back about an hour after meals, and was relieved by milk and alkalis. In addition he had attacks of colicky umbilical pain accompanied by borborygmi. His bowels were irregular, with a tendency to constipation, and he did not think he had lost weight. A barium meal confirmed the presence of a gastro-jejunostomy with much deformity suggesting active ulceration; there was an ulcer crater in the duodenum. The films also showed numerous fluid levels in the small intestine.

His abdomen was explored on April 26, 1955. There were a few adhesions to the back of the ulcer scar, but the remainder of the peritoneal cavity was free, and there was no intestinal obstruction caused by the adhesions. A gastro-jejuno-colic fistula was present, large enough to take a little finger. The viscera were separated and the fistula closed. There was a large ulcer on the posterior wall of the duodenum penetrating the pancreas, the crater being about 1 in. in diameter. The surrounding structures were so indurated and œdematous that dissection of the ulcer was regarded as too hazardous, and prepyloric closure was used. A routine partial gastrectomy was performed. On the third postoperative day his hæmorrhoids prolapsed, but his abdominal condition never gave rise to anxiety, and he went home on the thirteenth day after operation.

This patient had many signs and symptoms of fistula in addition to those of an ulcer; but some of these led to a diagnosis of subacute intestinal obstruction. Despite the activity of the fistula, his duodenal ulcer was undoubtedly causing symptoms, and the depth and extent of ulceration were sufficient to deter me from attempting to excise the first part of the duodenum.

### Discussion

During the period covered by my four cases of fistula, I have performed gastrectomy for anastomotic ulceration on twenty-three other occasions (twenty following gastro-enterostomy, one Polya gastrectomy, one Devine exclusion anastomosis, and one Billroth-I gastrectomy, this being case 3 above). The incidence of fistula in my cases was therefore about 15%.

Most workers say that the symptoms of fistula may be intermittent, but imply that this is uncommon. In Cases 1 and 2 the fistula symptoms had been absent for six and four months, and the patient in case 5 had had long intermissions. Disappearance of pain, with presumed healing of the ulcer, is usually recorded as a prominent feature, and is illustrated by case 3. Yet in three of my cases activity of the ulceration was the most striking feature, manifest by perforation into the peritoneal cavity, or penetration into the pancreas. It might be argued that reactivation of the ulcer might be expected with a silent fistula and a scarred anastomosis, but these three patients had definite symptoms of the fistula when their ulcers were active.

Many operations have been described for the treatment of gastro-jejuno-colic fistula, most of them comprising several stages. Improvements in anæsthesia, chemotherapy, and administration of intravenous fluids have occurred since many of these were described, and perhaps their originators would have less use for them now. Aird, however, still teaches that it is seldom possible to complete the treatment in one stage. Lowdon's series covered the years 1926–51 and many cases did not have the advantage of modern methods; even so, it is surprising that only two cases were considered fit for one-stage gastrectomy. Perhaps it is significant that the fistulæ were not recognised before operation in these cases.

I suggest that the terrifying picture of the effects of fistula is true of only the worst cases, or the later stages of the disease. If it were taught that mild cases are common, the diagnosis might be made more often at a stage when radical treatment is possible and safe. This treatment seems desirable both to prevent cachexia, and to avoid further complications of the still active ulceration.

### Summary

Five cases of gastro-jejuno-colic fistula are reported. Only one presented with symptoms due to the fistula; the other four had symptoms which could reasonably be ascribed to active peptic ulceration. All were fit for major operations.

The usual description of the condition resulting from such a fistula applies to severe or advanced cases. Mild cases or cases with intermittent symptoms are not generally recognised.

I am grateful to Mr. W. I. Wigg for information about case 2 up to 1951, and to Mr. C. Denley Clark for permission to include case 3.

#### REFERENCES

Aird, I. (1950) A Companion in Surgical Studies. Edinburgh.
Lowdon, A. G. R. (1953) *Brit. J. Surg.* **41**, 113.

## RUPTURE OF THE LIVER IN A NEWBORN INFANT

### WITH RECOVERY

J. L. GREAVES
M.D. Lond., M.R.C.P.
CONSULTANT PÆDIATRICIAN, TEES-SIDE GROUP OF HOSPITALS

RUPTURE of the liver has been found in 1·2% of 2000 newborn and stillborn infants examined at necropsy (Potter 1940). Yet few cases are diagnosed clinically, and so far as I can ascertain only 6 instances of survival have so far been recorded (Rubovitz [cited by Rogers 1934], Arden 1946, 1951, Benson and Prust 1953). I describe here a further instance of recovery.

### Case-record

The infant, a female, was born at 8.54 P.M. on Feb. 2, 1955; birth-weight 5 lb. 13 oz. The infant was delivered by an experienced midwife, and delivery was by the vertex and entirely normal. She was seen by the family practitioner shortly after birth when she appeared healthy, with a normal pink colour. The infant was put to the breast and sucked normally. Her condition gave rise to no anxiety and she made normal progress, apart from vomiting a little mucus once or twice, until 2.30 P.M. on Feb. 4 when she refused her feed and vomited. At 4.30 P.M. her mother noted a further change: the baby became pale, with blueness round the lips,

and she appeared to collapse. At 5 P.M. the family doctor saw the baby and called for a second opinion.

*On examination* at 5.30 P.M. the baby was very pale, breathing rapidly with some air-hunger. The abdomen was slightly distended and there was a faint bluish discoloration around the umbilicus. No shifting dullness could be elicited. No other abnormality was found; there was no evidence of blood in the vomit or on rectal examination or in the napkins. Intraperitoneal hæmorrhage was diagnosed, and the baby transferred to the children's unit at Middlesbrough General Hospital. Straight radiographs of the abdomen, taken with the infant in the horizontal and erect positions, showed no clear abnormality. No helpful alteration of radiographic shadows was demonstrated by moving the patient. (In retrospect the shadows in the peritoneal cavity were denser than normal.)

*Treatment.*—A transfusion of group-O rhesus-negative blood was set up, and the baby was seen in consultation with Mr. Ernest Grahame. The baby's condition improved greatly with the blood-transfusion; but it was decided to operate, to try to locate the site of bleeding and if possible to repair it.

*Laparotomy* (Mr. Grahame) was undertaken at 10 P.M. under local anæsthesia. On opening the peritoneum, which was purplish, fluid blood escaped, and about a quarter of a pint of blood was drained from the peritoneal cavity. Blood was found to be coming from a tear, about 1 in. long, in the lower border of the right lobe of the liver, which seemed very friable. The bleeding was controlled by inserting three catgut sutures, and the abdomen was closed in layers with drainage.

*Further treatment and progress.*—The baby was given 'Synkavit' 10 mg. and streptomycin 100 mg. twice daily by intramuscular injection, and penicillin 0·25 mega-unit six-hourly by intramuscular injection. The drain was removed after twenty-four hours. Postoperative recovery was complicated by moderate abdominal distension and vomiting of some bile-stained fluid, which made it necessary to continue the intravenous drip until Feb. 8. The baby was gradually got on to a normal feed for her age and was finally discharged on March 2, weighing 5 lb. 15 oz. and gaining weight satisfactorily. The baby subsequently made good progress, gaining weight normally without vomiting. The wound is soundly healed.

### Discussion

There is some divergence of opinion as to whether rupture of the liver is especially common in premature, normal, or post-mature infants.

In 15 cases reported by Stein and Wright (1953) there was an equal distribution between premature and full-term infants. In Arden's (1951) series, however, the average weight of the infants was 9 lb. 6 oz., and their large size appeared to be the only ætiological factor. In the majority of cases delivery was spontaneous and normal, with no obvious trauma to the infant.

During delivery the liver is more commonly injured than any other intra-abdominal organ (Ehrenfast 1931), probably because its free border is unprotected by the rib margin in most newborn infants. A subcapsular hæmatoma forms and gradually enlarges, and if the bleeding does not stop this hæmatoma ruptures through the liver capsule, resulting in sudden loss of blood with collapse and shock (Potter 1940, Arden 1951). In the present case the infant had lost over half her blood-volume into the peritoneal cavity.

The clinical picture is usually quite clear (Tow 1937, Arden 1946, 1951). The infant, previously apparently well, suddenly collapses some forty-eight hours after birth, with pallor and rapid breathing going on to air-hunger. Sometimes there is an area of dullness down the right side of the abdomen, tending to confirm that the liver is the injured organ.

Immediate blood-transfusion is the first step in treatment; and this may be required so urgently that there is no time for full cross-matching. When the immediate shock has been overcome, laparotomy can then be undertaken. Arden (1951) now recommends treatment by transfusion alone, but I believe that it is wiser to locate the site of bleeding and if possible control it. Moreover, rupture of the liver may be closely mimicked by other disorders—notably volvulus of the small gut (though with volvulus the onset is usually within the first twenty-four hours of life). Accordingly laparotomy is important in order to confirm the diagnosis as well as to apply local hæmostasis. In the present case vomiting and some abdominal distension were the only postoperative complications, and this has been noted by others (Arden 1951). Retained intraperitoneal blood is probably the cause.

### Summary

In an infant who collapsed forty-four hours after birth intraperitoneal hæmorrhage was diagnosed. At laparotomy a tear in the liver was sutured. The infant recovered completely.

I should like to thank Mr. Ernest Grahame for carrying out the operation with such success.

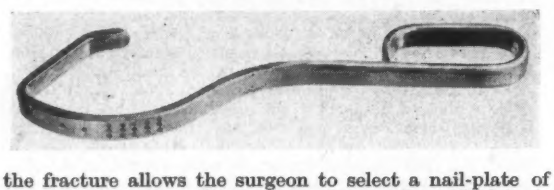
#### REFERENCES

Arden, F. (1946) *Med. J. Aust.* i, 187.
— (1951) *Ibid*, ii, 632.
Benson, C. D., Prust, F. W. (1953) *Surg. Clin. N. Amer.* **118**, 7.
Ehrenfast, H. (1931) Birth Injuries of the Child. New York p. 286.
Potter, E. L. (1940) *J. Amer. med. Ass.* **115**, 996.
Rogers, G. (1934) *Amer. J. Obstet. Gynec.* **27**, 841.
Stein, F. E., Wright, L. T. (1953) *Harlem Hosp. Bull.* **6**, 32.
Tow, A. (1937) Diseases of the Newborn, p. 108.

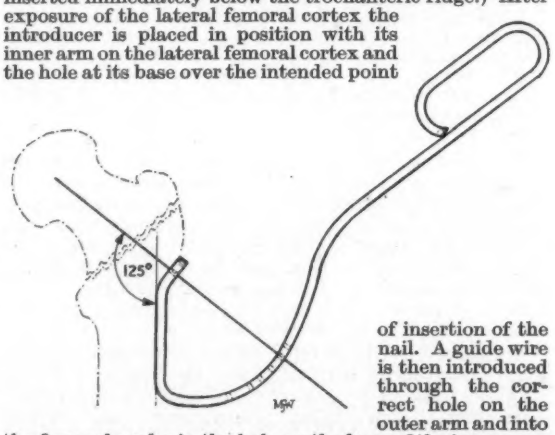
## New Inventions

### AN INTRODUCER FOR USE WITH THE CAPENER NAIL-PLATE

THIS instrument allows a guide wire to be inserted so that the angle between the wire and the lateral femoral cortex is the same as that of the selected nail-plate. The anteroposterior radiograph taken after reduction of



the fracture allows the surgeon to select a nail-plate of the correct angle. (It is assumed that the nail-plate is inserted immediately below the trochanteric ridge.) After exposure of the lateral femoral cortex the introducer is placed in position with its inner arm on the lateral femoral cortex and the hole at its base over the intended point




of insertion of the nail. A guide wire is then introduced through the correct hole on the outer arm and into the femoral neck via the hole on the base of the inner arm. The instrument is removed, and the position of the wire is checked by anteroposterior and lateral radiographs. If this is satisfactory, the nail is then inserted over the wire.

I am most grateful to Mr. R. F. Somerville, of Down Bros., for his valuable assistance.

J. S. BATCHELOR
F.R.C.S.

London, W.1

# Reviews of Books

## The Hemorrhagic Disorders

MARIO STEFANINI, M.D., associate professor of medicine, Tufts University, Boston; WILLIAM DAMESHEK, M.D., professor of medicine in the university. New York and London: Grune & Stratton. 1955. Pp. 368. 70*s*.

BLOOD-CLOTTING and its disorders have been very closely studied of late, and Biggs and Macfarlane have provided a standard text on human blood coagulation. But it is fair to say, as do the authors of this book, that previous works deal mainly with the laboratory aspects and only incidentally with the clinical side of the subject; and that blood-clotting studies "represent only one leg of a four-legged stool, of which the other legs are the vascular, the platelet, and the fibrinolytic mechanisms." Dr. Stefanini and Dr. Dameshek deal with all four sides of hæmorrhagic diseases, and their approach is that of the clinician who regards clinical investigation with laboratory studies as only one phase in the management of the patient. The physician who wants a modern guide to hæmorrhagic diseases will find everything he needs in this well-written and reasonably short book.

It begins with a very necessary glossary of the terminology adopted, with the corresponding names used by some others. The opening pages deal with the details of normal hæmostasis, and in this section and the following one effective use is made of tables and figures. The eleven chapters on the various types of hæmorrhagic disease form the bulk of the book, and the illustrations are good, except for some lurid colour plates.

Among many interesting points, we are glad to see the term "pseudo-hæmophilia" used only for a congenital vascular abnormality; there is an interesting section on the differential diagnosis between telangiectases and "spiders"; the authors prefer corticotrophin to cortisone for the treatment of anaphylactoid purpura; they distinguish sharply between acute self-limited idiopathic thrombocytopenic purpura and the chronic relapsing form; they give an interesting list of "outmoded" forms of treatment of this disease, while pressing the value of platelet transfusions; and there is a sensible appraisal of the various forms of treatment suggested for hæmophilia. All the clinical aspects of hæmorrhagic diseases are, in fact, dealt with in a stimulating manner.

Recommendations on treatment are usefully collected into a single chapter. In another the hereditary aspects are discussed, and the authors repeat here their claim to be able to detect some female hæmophilic carriers by studying the electrophoretic pattern of their serum-proteins. A short but adequate appendix describes the techniques used, and a bibliography of 753 references shows that the world literature has been fully consulted.

## Salivary Gland Tumours

DONALD E. ROSS, M.D., F.R.C.S., chief surgeon, Ross-Loos Medical Group, Los Angeles. Springfield, Ill.: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1955. Pp. 86. 54*s*.

THERE are two main types of monograph, sometimes combined—the comprehensive authoritative review, and the record of personal experience amplified and illustrated more than is possible in an article in a journal. This book is rather in the second class.

For example, the introductory chapters on the history of the subject and on histogenesis are altogether too brief for a comprehensive review. Again, there is no mention, under complications, of gustatory sweating (Frey's syndrome) as a complication of parotidectomy, nor of partial tarsorrhaphy in the treatment of facial paralysis. On the other hand, in the later chapters the author goes very fully into the anatomy and technique of parotidectomy and, though some of the many views of the bony skull hardly seem relevant, detailed descriptions of the technique of parotidectomy with preservation of the facial nerve are sufficiently uncommon to make this contribution welcome.

The short chapter analysing Dr. Ross's own material is also valuable, particularly for the further evidence of the rarity of permanent facial paralysis after parotidectomy, and for the section on the possibility of preservation of the facial nerve in early carcinoma. But perhaps these points might have been better made by an article in a journal.

There is a good bibliography with nearly 400 references, but it is surprising, in view of the French contribution, to find little reference to Redon's work.

In his foreword, the author aptly sums up the modern approach to parotid tumours: "Physicians do not realise adequately the serious nature and the potential danger of malignancy in these tumours. There is a deep dread of injuring the facial nerve. This leads to procrastination, and there is an average duration of seven years before surgical intervention . . . Certainly, all should realise that these tumours can be removed adequately, and yet the facial nerve can, except in rare cases, be saved."

## The Princes in the Tower and Other Royal Mysteries

Sir ARTHUR S. MACNALTY, F.R.C.P., F.R.C.S. London: Christopher Johnson. 1955. Pp. 212. 18*s*.

DID Richard III murder the Princes in the Tower? Or was the villain Henry VII? Which censor of the Royal College of Physicians was racked twice in the Tower almost to death? Which St. Bartholomew's Hospital physician was found guilty of attempting to poison Queen Elizabeth I and hanged, drawn, and quartered at Tyburn? Was it a trumped-up charge? Did the son of Louis XVI die in prison or had a rachitic, tuberculous child been substituted? These questions and others are raised in this modern examination of ten historical crimes that concerned the royal houses of England, Spain, France, Sweden, Denmark, and Russia. They make easy if unhappy and sometimes harrowing reading. Stress is laid on what little medical evidence is available. Several of the mysteries remain unsolved, but Sir Arthur concludes that the death of the youthful Caroline Matilda, Queen of Denmark, was due in all probability to cerebrospinal meningitis and not to poison. Whether or not he is right in his conclusions about the murderer of the Princes in the Tower must be left to readers to decide.

## Genital Prolapse and Allied Conditions

PERCY MALPAS, CH.M., F.R.C.S., F.R.C.O.G., surgeon to the Women's Hospital, Liverpool. London: Harvey & Blythe. 1955. Pp. 199. 47*s*. 6*d*.

THE declared aim of this book is to clarify and systematise the author's experience of some 7000 operations and cases of prolapse.

It covers the anatomy, ætiology, varieties, and symptoms of prolapse, with chapters on the non-operative management, the Fothergill operation, vaginal hysterectomy, and other related techniques. There are also chapters about the complications of operation, disturbances of micturition associated with genital prolapse, the rectal complications of prolapse, and retroversion of the uterus.

The book seems to have been written mainly for the author's own benefit, and it is therefore likely to appeal only to gynæcologists of experience. It contains much wisdom, and many readers will be refreshed by the thoughts and opinions, even though they may disagree with them. But somehow it is disappointing: Mr. Malpas has not restricted himself to matters within his own experience, as he implies in his introduction, for he has included considerable passages that belong to the experience of others, and this dilution has not always strengthened the text.

The illustrations are poor: many have been borrowed, and a few are not clear; some, though clear, are ill chosen, and others have little or no obvious use.

## Les cancers du côlon

M. ROUX, professor in the faculty of medicine, Paris; F. CARCASSONNE, professor in the faculty of medicine, Marseilles; R. LE CANUET, radiologist, Hospital of the Pasteur Institute, Paris. Paris: Masson. 1955. Pp. 368. Fr. 3200.

THIS monograph presents on traditional lines a complete survey of the surgical implications of cancer of the colon.

The clinical manifestations are admirably presented and the fifty pages devoted to radiological appearances contain excellent reproductions of radiographs, with many good explanatory diagrams. Naturally the greater part of the

work is devoted to operative technique and details of pre-operative and postoperative care; here the illustrations are very clear, though in contrast to the delicacy of the line drawings in the previous chapter, they have that harsh quality not uncommon in medical illustrations today. The authors' own results are compared with those from other centres, and they are given in a way which permits an evaluation of operative method as well as the significance of the type of tumour, its extent, and complications. This chapter rightly ends by considering the effect of the surgeon's experience on survival-rate. It is surprising that indications for operation are not considered until the final chapter.

This is a painstaking work with which those especially interested in colon cancer (rectal lesions are excluded) should be acquainted.

### The Spine

*A Radiological Text and Atlas.* BERNARD S. EPSTEIN, M.D., chief, Department of Radiology, The Long Island Jewish Hospital, New York. London: Henry Kimpton. 1955. Pp. 539. £6.

Dr. Epstein has approached his subject in an original way which may well prove to be a valuable method of teaching. Instead of producing an ordinary descriptive textbook of radiological appearances, he gives an extended account of the historical, ætiological, pathological, and clinical aspects, and often leaves the reader to make his own deductions about the radiographs. All known disorders of the spine and all the diseases which can affect it have been included.

The text is based largely on the literature: there are about 1500 references in the bibliography, and many are quoted at some length. The author's own opinion (and his experience must be very wide) tends to get lost in this great mass of quotation.

The illustrations unfortunately are disappointing both in quality and number. The detail is poor, and many of the films have been too far reduced in size. Many conditions described in the text are not illustrated.

Nevertheless the book is a very useful reference to the literature for both physician and surgeon, and it should be a great help to the radiologist-in-training whose clinical knowledge is limited.

### From Witchcraft to Antisepsis

DOUGLAS GUTHRIE, M.D., F.R.C.S.E., lecturer on the history of medicine, University of Edinburgh. Lawrence: University of Kansas Press. 1955. Pp. 53. $1.50.

Two very readable and contrasting lectures, one on witchcraft and the other telling the oft-told story of Lister and his achievement, may appear, as the author says, to have little in common at first sight. "Yet each represents the origin and growth of an idea; the first, magical, medieval, and detrimental to mankind; the second, logical, scientific, and supremely beneficial. Witchcraft and Antisepsis are as poles apart, the very antithesis of each other; yet, from both, we may learn lessons which are of interest and of value in relation to modern medicine." These were the 1955 Logan Clendening lectures on the history and philosophy of medicine.

### La carence de soins maternels

JENNY AUBRY. Médecin des Hôpitaux de Paris. Paris: Presses Universitaires de France. 1955. Pp. 188. Fr. 720.

THIS study of the child separated from its mother was carried out by a team consisting of pædiatricians, a psychiatrist, psychologists, infant teachers, and social workers, working under Dr. Aubry's direction at a reception centre of the Assistance Publique de la Seine.

The centre, La Fondation Parent de Rosan, houses 60 children aged one to four, who are admitted after a stay of some days at l'Hôpital Saint-Vincent-de-Paul, and stay for a few weeks or several months. This book records the methods of observation and testing, and the results observed; and graphs illustrate the effect on physical and psychological development of long or short deprivation at various ages. Case-histories of children who needed prolonged psychological treatment are used to show how variable the damage can be.

In the final chapters Dr. Aubry describes the practical difficulties in avoiding separation of the young child from its mother, and some measures for giving those unavoidably separated the best possible care either in an institution or, preferably, in a foster-home. A start has been made in placing seriously deprived children directly with selected foster-mothers rather than giving them specialised treatment in the institution, despite the high cost. It is to be hoped that this step will have the success it deserves.

### Ultrasonic Engineering

*With particular reference to High Power Applications.* ALAN E. CRAWFORD. London: Butterworths Scientific Publications. 1955. Pp. 344. 45*s*.

HIGH-FREQUENCY vibrations beyond audibility have been used to fragment bacterial cells and liberate their enzymes or bacteriophage particles for further study, to make localised brain lesions in experimental animals, to detect tumours in various tissues, and to treat a great assortment of physical ills. According to this book, in 1951 there was an ultrasonic generator for every six practising physicians in Western Germany alone. So far, however, there is very little objective evidence for any clinical value of ultrasonics, and their application mainly lies in many fields of industry—in emulsification and agglomeration processes, and in chemistry and metallurgy. This book explains clearly, with profuse illustrations, what ultrasonics are and how they may be produced and used. Its medical value lies in any new ideas it may give medical readers.

---

**Thoracic Surgical Management** (2nd ed. London: Baillière, Tindall, & Cox. 1955. Pp. 216. 21*s*.).—The handbook by Mr. J. R. Belcher and Dr. I. W. B. Grant which has proved so valuable to housemen and others has rapidly come to a second edition, in which certain improvements may be noted. The authors' aim is to provide a detailed account of preparation and after-treatment for thoracic surgical operations, and to illustrate the possible complications. The instructions are precise and sufficiently dogmatic to leave no room for confusion, and the diagrams are adequate. In short, it is an admirable bedside book for the houseman who is suddenly thrust into the active practice of thoracic surgery.

**The Numbers of Man and Animals** (Edinburgh: Oliver & Boyd. 1955. Pp. 152. 15*s*.).—In 1954 the Institute of Biology held a conference of specialists in different subjects connected with the numbers of man and animals.[1] This book reprints the main papers and gives what the editors, Prof. J. B. Cragg and Mr. N. W. Pirie, F.R.S., describe as "a slightly idealised version" of the discussion which followed. The medical contributors were Prof. A. L. Banks, Prof. L. S. Penrose, F.R.S., and Lord Boyd Orr, F.R.S.

**Biochemistry of the Developing Nervous System** (New York: Academic Press. London: Academic Books. 1955. Pp. 537. 92*s*.).—The proceedings of the first International Neurochemical Symposium,[2] held at Oxford in July, 1954, have now been published under the editorship of Dr. Heinrich Waelsch who, with Prof. Joel Elkes, contributes a preface.

**Short Textbook of Surgery.** (6th ed. London: J. & A. Churchill. 1955. Pp. 628. 37*s*. 6*d*.).—Prof. C. F. W. Illingworth's book is deservedly popular because it does great service to students by covering the surgical field in 600 pages, packed tight with orderly facts. Moreover, for the new edition, the author has had the courage to discard what is becoming irrelevant; thus, those classical infections which are seldom seen today—syphilis, gonorrhœa, erysipelas—are now given little room. As usual, there are plenty of good illustrations.

**Biochemistry of Vitamin $B_{12}$** (London: Cambridge University Press. 1955. Pp. 123. 20*s*.).—Under this title the Biochemical Society has published, as no. 13 of their symposia, the proceedings of the meeting held in London in February. The editor is Prof. R. T. Williams, D.SC.

1. See *Lancet*, 1954, ii, 743.
2. *Ibid*, p. 234.

# THE LANCET

*LONDON: SATURDAY, DEC. 10, 1955*


## Needle Biopsy of the Kidney

NEEDLE biopsy of the liver is now a well-established and relatively safe means of diagnosis. In a recent review of over 20,000 hepatic biopsies [1] the mortality-rate was said to be only 0·17%; but SHERLOCK [2] considers that 0·3% is probably more accurate, since deaths directly caused by diagnostic procedures are often not published. Needle biopsy of the kidney, although it is being extensively used in many centres, is not so firmly established. The value of renal biopsy was first shown by CASTLEMAN and SMITHWICK,[3] who took samples of kidney tissue during the operation of lumbar sympathectomy for hypertension. They found that in 28% of patients there were no hypertensive changes in the renal vessels, although these changes were always present in post-mortem specimens from hypertensive patients. This observation showed that the high blood-pressure often preceded structural changes in the vessels. Percutaneous needle biopsy of the kidney was first extensively used by IVERSEN and BRUN.[4] The operation was performed with the patients in the sitting position, and suction was applied during the removal of renal tissue. The results have been reviewed by RAASCHOU,[5] who reported success in only 38% of attempts. When satisfactorily carried out, this method produced a thin cylinder of renal tissue, averaging 10 mm. in length and containing about ten glomeruli. Last year KARK and MUEHRCKE [6] described an improved method of renal biopsy, and now, in collaboration with PIRANI and POLLAK, they have recorded the results in 200 patients.[7–9] These biopsies were performed with the patient prone, and a modified Vim-Silverman needle was used. Kidney tissue was removed by the thin cutting blades of this instrument without the need of suction. Results were satisfactory in 93% of cases. KARK et al.[9] believe that these improved results are due to a more accurate method of localising the kidney. The surface marking of the lower and outer pole of the right kidney was first determined by X-ray examination. The depth of the posterior surface of the kidney was defined by a thin exploring needle, which was slowly introduced until the movement of the kidney on respiration produced an equivalent swing of the protruding part of the needle. Although a needle biopsy can under exceptional circumstances be performed on the left kidney, it is judged to be more dangerous because of the risk of damaging the spleen or large vessels.

Needle biopsy should not be used when there is any tendency to bleeding, when there is only a single kidney, or when there is a possibility of renal cysts, hydronephrosis, pyonephrosis, renal neoplasm, or aneurysm of the renal artery. It is also contra-indicated where there is calcification of vessels, or in uræmia with a steadily rising blood-urea. In expert hands the method appears to be as safe as liver biopsy. Over 800 renal biopsies have now been reported and serious complications have been uncommon. ALWALL [10] reported a case in which surgical shock and fatal anuria followed biopsy, and PARRISH and HOWE [11] described a patient who had a large retro-peritoneal hæmatoma that required operation. With their new method KARK and his colleagues have had no complications more serious than transient hæmaturia, and temporary renal colic due to the passage of clots. In 1 patient the hæmorrhage was severe enough to require transfusion. If bleeding should be serious, modern experience in the management of traumatic injuries of the kidney [12] suggests that conservative measures are best. Obviously, needle biopsy of the kidney, like many other means of investigation, is not free from risk, and for the time being it should probably be undertaken only in hospitals where it has been made a special study. There seems little doubt, however, that it will presently be used more widely and that it will further our knowledge of the pathology, prognosis, and evolution of renal disease. For instance, several patients have already had as many as four successive biopsies, giving detailed information of progressive renal disease which could not have been obtained by other means. This is not, however, an adequate justification for a potentially dangerous operation; and biopsy should be used only when the information it gives will be of direct advantage to the patient, and not merely a rather academic addition to medical knowledge.

KARK and his colleagues [8 9] have described a form of nephritis which can be diagnosed only by renal biopsy. They have called it "subacute bacterial nephritis," and they have already successfully treated it in 5 patients. These patients all had proteinuria and depressed renal function, but they showed no evidence of pyelonephritis. Pathologically, there were interstitial inflammatory changes around the glomeruli, with actual necrosis in some areas. Antibiotics appropriate to the organism cultured from the biopsy specimen stopped the proteinuria and improved renal function. Subsequent biopsies showed considerable resolution of the lesions. Biopsy culture seems better than urine culture for identifying the organism responsible for acute and chronic pyelonephritis. KIPNIS et al.[13] have taken biopsies in 13 cases of pyelonephritis and there was no evidence afterwards of exacerbation or extension of the infection. The method will probably be most useful in urinary infections where several distinct organisms are obtained by urine culture; antibiotics should preferably be directed at the organisms obtained from renal tissue. Biopsy has also proved of great value in the diagnosis of renal amyloidosis, polyarteritis nodosa, and lupus erythematosus. Secondary amyloidosis may often resolve if the primary disease can be eradicated, and therefore accurate assessment of the renal changes may be essential in planning treatment. Unfortunately,


1. Zamcheck, N., Sidman, R. L. *New Engl. J. Med.* 1953, **249**, 1020.
2. Sherlock, S. Diseases of the Liver and Biliary System. Oxford, 1955; p. 75.
3. Castleman, B., Smithwick, R. H. *J. Amer. med. Ass.* 1943, **121**, 1256.
4. Iversen, P., Brun, C. *Amer. J. Med.* 1951, **11**, 324.
5. Raaschou, F. The Kidney. London, 1954; p. 15.
6. Kark, R. M., Muehrcke, R. C. *Lancet*, 1954, **i**, 1047.
7. Muehrcke, R. C., Kark, R. M., Pirani, C. L. *New Engl. J. Med.* 1955, **253**, 537.
8. Muehrcke, R. C., Kark, R. M., Pirani, C. L. *J. Urol.* 1955, **74**, 267.
9. Kark, R. M., Muehrcke, R. C., Pirani, C. L., Pollak, V. E. *Ann. intern. Med.* 1955 **43**, 807.
10. Alwall, N. *Acta med. scand.* 1952, **143**, 430.
11. Parrish, A. E., Howe, J. S. *J. Lab. clin. Med.* 1953, **42**, 152.
12. Sargent, J. C., Marquardt, C. R. *J. Urol.* 1950, **63**, 1.
13. Kipnis, G. P., Jackson, G. G., Dallenbach, F. D., Schoenberger, J. A. *Arch. intern. Med.* 1955, **95**, 445.

renal involvement in the collagen diseases does not often respond satisfactorily to cortisone or corticotrophin, and therefore biopsy is at present of less direct value to the patient. BJØRNEBOE et al.[14] found that biopsy was useful in predicting the response of the nephrotic syndrome to cortisone or corticotrophin; patients with normal glomeruli or with only slight glomerular involvement are more likely to improve. But a therapeutic trial would give the same information with less disturbance to the patient. MILNE[15] has suggested that renal biopsy may help in the differential diagnosis between the recently described condition of primary aldosteronism[16] and hypokalæmic paralysis secondary to primary renal disease. This differentiation is of especial importance since aldosteronism requires surgical treatment, whilst hypokalæmia due to renal disease can only be corrected by the appropriate potassium supplements.

There are other interesting possibilities, but it seems unlikely that renal biopsy will achieve the importance that liver biopsy is now assuming. Many lives have been saved by liver biopsy in the differential diagnosis of prolonged jaundice; but accurate differential diagnosis of renal disease is rarely of such immediate and crucial importance.

## Law and the Mental Patient

THE task of providing care and treatment for the mentally ill is certainly complex; yet hardly as complex as the laws designed to ensure that it is done. Our own legislation, a plant of slow growth, cannot be said to have flowered yet; and in other countries equally backward vegetation is struggling towards the light. So much is clear from the survey[17] of existing legislation in 40-odd countries, lately published by the World Health Organisation. It is a useful handbook, nevertheless, for any country not too proud to profit from the experience of others.

The earliest laws for the custodial care of the insane were designed to protect society, and introduced the danger of arbitrary detention. Towards the middle of last century, however, several countries were devising laws to protect the rights of mental patients. In some countries the duty of protection was placed on the medical or administrative authorities, in others solely on judicial authorities; and these arrangements have held, in the main, until now. Whatever the authority, the certified patient becomes subject to legal disabilities: he cannot control his property, make a will, or exercise paternal rights; and even today in some places provisions for placing the mentally ill in hospital are to be found only in laws dealing with civil incapacity. Such arrangements naturally do not favour early admission and treatment; and the introduction of voluntary admission has been a great step forward. In some countries, including our own, it suffices for the patient to apply (usually in writing) to be admitted for treatment as a voluntary patient; in others a medical certificate, or certificates, must be supplied; while others again require the signature of justices of the peace or of witnesses. Obviously the simpler the procedure the better: it is not clear, in any case, why a patient voluntarily seeking treatment in a hospital need sign anything at all. Indeed some of our mental hospitals now have wards which accept, without any formality, "non-statutory" patients who come and go like the patients of general hospitals—a promising idea, well worth exploring further.

It is, of course, the patient too ill to consent to treatment who presents the lawmakers with their greatest problem. In some countries a patient may be received into hospital, without his consent, on medical certification alone. This type of admission has many of the advantages of voluntary admission: it makes early treatment possible, and does not require the intervention of lay officials, which always carries a stigma. Safeguards—such as notification of admission, inspections, rights of appeal, and thorough medical examination, often by specially designated experts—minimise the risks of a sane person being admitted against his will. In England we use the method only in the case of patients admitted for "temporary" treatment—patients that is, who are expected to recover within a reasonable time, but are unable, at the time of admission, to say whether they would like treatment or not. Used in this sense, "temporary" is taken in most countries to mean a period of six months, at the end of which the patient—unless he has meanwhile recovered sufficiently to become a voluntary patient—must be discharged or certified. But in Northern Ireland an ingenious and humane law, to which we have previously drawn attention,[18] enables all patients other than voluntary patients to be admitted with "temporary" status. Moreover, the initial period of treatment is for a year; and it can be extended for another year, or even longer, if hopes of recovery are still good. This has made it possible to avoid certification altogether in a large proportion of cases, and always to postpone it for as long as hopes of an early recovery remain. In Italy, Peru, Spain, and Uruguay *all* involuntary patients are admitted in the first place for observation—surely a sensible idea.

In many countries the usual method of involuntary admission is by judicial order; and there are several ways in which the trauma can be enhanced. Thus in some provinces of Canada the patient may be apprehended by a court warrant; in some American States special commissions appointed by a judge, or standing commissions, either make the order for reception or report their findings to a court for a final decision; and in one State the patient's mental condition is decided at trial by jury. Such measures mean that in the public mind mentally ill patients tend to be classed with criminals, and this tendency is increased where patients are lodged in gaol while awaiting inquiry into their mental condition—as may happen in 37 of the United States. In 40 States, moreover, the patient may be transported from gaol to hospital by the police.

The World Health Organisation's expert committee on mental health[19] think that, in general, purely legal considerations have been given too much weight, and medical considerations too little. Most existing legislation, they believe, is concerned too much with placing checks on the mental patient and his physicians, and too little with the public's responsibility

14. Bjørneboe, M., Brun, C., Gormsen, H., Iversen, P., Raaschou, F. *Acta med. scand.* 1952, **266**, suppl. 249.
15. Milne, M. D. *Proc. R. Soc. Med.* 1955, **48**, 780.
16. Conn, J. W. *J. Lab. clin. Med.* 1955, **45**, 3.
17. Hospitalisation of Mental Patients. Geneva: World Health Organisation. H.M. Stationery Office. 1955. Pp. 100. 6*s.* 6*d.*
18. *Lancet*, 1954, i, 1332.
19. *Wld Hlth Org. techn. Rep. Ser.* no. 98. 1955.

for providing services for the mentally ill: "It does little to foster a positive approach to mental health." The psychiatric hospital can be either the best or the worst possible thing for a patient—a therapeutic community or an instrument of desocialisation. Good treatment depends on a humane and well-trained staff, and in all countries the first necessity for which the law should provide is the recruitment and training of such staff. The number of hospital beds should depend on the number of people to staff them: "Good psychiatrists without specialised hospital establishments would render greater service to patients and to the community than psychiatric hospitals without adequate professional staff."

Naturally the law must provide for the treatment, without their consent, of patients who are dangerous; but it should also guarantee them guardianship and medical supervision. The type of guardianship proposed by the committee would be flexible, providing advice for patients capable of giving valid consent on the management of their private affairs, assisting those who are capable only of giving an opinion on such matters, and acting on behalf of those who are wholly incapable in this respect. A patient should have ready means of appeal at any time after involuntary admission; and, whatever the composition of the body which hears the appeal and, if necessary, authorises compulsory detention, its purpose should be to pronounce on the *legality* of the detention: it need not and should not be required to certify that a patient is insane or mentally subnormal. "The distinction between the authorisation of detention and the certification of an individual's state of mind is an important one." The committee also favour much more flexible arrangements for the discharge of patients, believing that the more widely, within reason, such powers are distributed the better. The next-of-kin should have, as here, power to discharge a patient, subject only to a veto from the medical superintendent on the grounds that the patient is dangerous to himself or others; and the next-of-kin should also have the right of appeal against such a veto. The medical superintendent, the medical inspectors of the health authority, the hospital management committee, and the local or central health authority should all, the committee hold, have the right to discharge patients: for nothing deters people from seeking early treatment more effectively than the fear that once one goes into a mental hospital it is difficult to get out.

The committee find in almost every country conflicting attitudes to the mentally ill: in some of them the laws are advanced while public opinion remains primitive; in others psychiatric care is well developed and legislation backward. They suggest that while new legislation is going forward, the old laws should be retained and allowed imperceptibly to fall into abeyance, or else that legislation should provide for a permanent body to be responsible for revising, at stated intervals, the laws affecting mental patients. Though this second proposal would hardly be consistent with British constitutional practice, we have other means of reaching the same end; and our laws relating to certification and detention of the mentally ill are at present being reviewed by the Royal Commission presided over by Lord PERCY of NEWCASTLE.[20]

20. *Lancet*, 1954, i, 353.

# Annotations

## DETERGENTS AT LARGE

THE regulations which assess the quality and cleanliness of milk by statutory tests have without doubt been of benefit to the consumer, but when these qualities are measured by the simple yardstick of "pass" or "fail" it is easy to forget the complexity of the biological mechanisms involved. Milk of an unusually high quality may be as proper a subject of inquiry as that which is judged unfit to be drunk. Until a recent change in the regulations, the pasteurised milk supplied to the hospitals of Paris should not have contained more than 100,000 organisms per ml. (i.e., the same standard which applied formerly in England and Wales). Routine testing showed that, in fact, a surprisingly large number of samples yielded bacterial counts so far below this figure that the presence of some disinfectant substance was suspected.[1] The most probable was a detergent used in cleaning the milk plant, especially one of the quaternary ammonium compounds which are powerful bactericidal agents and enjoy considerable popularity. Like all detergents these are not easy to remove from surfaces of glass or metal without very thorough rinsing. Using a simple but not entirely specific test, the investigators showed that 12% of milk cans contained traces of substances which might have been of this nature.

We know of no similar observations in this country. The chemical detection of detergents is not easy and the quaternary ammonium compounds are usually reckoned too costly for use in the dairy. Evidence for and against their toxicity in small doses is scanty. Chemical technology is in fact bounding forward at such a pace that new compounds whose properties are but half known are on the market within a short time of their discovery. Seldom has the buyer or the seller the scientific knowledge to form any estimate of the possible risk from some secondary action. While the expert is in the position to forecast that a compound might cause dermatitis or cancer, the public must rely upon the protection of the common law and the good conscience of the manufacturer—and to dismiss the second as valueless is both foolish and unjust. The greatest danger from compounds new to our experience arise not when they are used for their designed purpose but when by accident or oversight they penetrate where they are unexpected and unwanted—to this milk, for example. Penicillin used for treating bovine mastitis has given the cheese-maker many headaches by killing his starter cultures. It is to be hoped that overzealous sanitation in the milk factories will not make unwanted (and illegal [2]) additions to our morning cup of tea.

## ASPIRINS FOR EMPHYSEMA?

SOME emphysematous patients puff and blow for many years without much deterioration; others decline into respiratory acidosis and anoxic heart-failure with scarcely a sigh. Measurement of the respiratory response of such patients to induced changes in arterial gas tensions and pH confirms the clinical inference that the sensitivity of central respiratory control is reduced.[3] One aspect of decreased sensitivity to carbon dioxide, which attracted attention some years ago, is the tendency for oxygen therapy to aggravate hypercapnia and respiratory acidosis, with consequent drowsiness or even coma. Many physicians became unduly timid about giving oxygen to anoxic patients, but recent work [4] suggests that, in acute respiratory insufficiency, the acute anoxia

1. Charonnat, R. *Bull. Acad. Méd. Paris*, 1955, **139**, 450.
2. Milk and Dairies Regulations, 1949, IX, 26, 6 *c*. H.M. Stationery Office.
3. Prime, F. J., Westlake, E. K. *Clin. Sci.* 1954, **13**, 321.
4. Westlake, E. K., Simpson, T., Kaye, M. *Quart. J. Med.* 1955, **24**, 155.

may itself be responsible for the central depression which may recover completely under proper oxygen therapy. This work supports the view [5] that these patients, who have become severely anoxic without time for acclimatisation, are in urgent need of oxygen, and that every effort should be made to restore them to a reasonable colour. Patients with chronic anoxia present a different problem since their need for oxygen is less urgent and their central depression less labile.

Of the various components into which respiratory insufficiency may be analysed,[6] central depression, although a common and occasionally the leading abnormality,[7] is perhaps the least understood. As even the chronic form has no manifest structural basis, there is at least the hope of reversing it, and two drugs have recently been studied to this end. The first is the carbonic-anhydrase inhibitor, acetazolamide, whose continued administration for periods of several months has recently been reported.[8] Doses of 500 mg. a day were partially successful in sabotaging the kidney's attempts at compensating the respiratory acidosis; consequently the plasma-bicarbonate fell, the acidosis increased and, presumably through increased ventilation, arterial $pCO_2$ fell and $pO_2$ rose slightly. There was no restoration of central sensitivity to carbon dioxide, nor in a complementary study [9] was there increased tolerance to oxygen. It is not certain that this purchase of a modest reduction of hypercapnia at the cost of further acidosis is a good biochemical bargain, and we are not told what the patients felt about it. Prolonged administration of acetazolamide entails a hazard of potassium depletion,[10] and few physicians will feel tempted on present evidence to use it in this way.

The second drug to be considered is salicylic acid. The hyperpnœa produced by large doses is familiar, and is now known to be due to a direct stimulation of the respiratory centre.[11] The result is normally a hypocapnia and respiratory alkalosis mitigated by a decrease in plasma-bicarbonate brought about by the kidney. These changes are the reverse of those found in central respiratory depression in which it is to be expected that salicylates would tend to restore normal values; and this has been found to be so in a few patients given 3–7 g. a day of aspirin.[12] This dosage is not prohibitively high, but is likely to produce side-effects, and the patients became irritable and some developed tremor. Tenney and Miller,[13] in recent work on the pharmacology of salicylates, draw attention to a property previously reported but usually overlooked—namely, the stimulation of oxygen consumption. An infusion of sodium salicylate may double oxygen consumption; oral dosage may produce a sustained increase of about 20%. This may well limit its use in patients with respiratory insufficiency who are very sensitive to changes in metabolic needs.

For patients with chronic respiratory insufficiency with prominent central depression, evidenced by hypercapnia with little respiratory distress, stimulation with aspirin may be worth trying. Acetazolamide may be of value as a short-term adjuvant in running down plasma-bicarbonate. There seems a fair prospect of objective improvement in blood gas-tensions and pH. Whether the patients will be grateful is doubtful, since, as Dornhorst [6] pointed out, successful reversal of central depression may prolong life but will almost certainly increase dyspnœa.

5. *Lancet*, 1953, i, 380.
6. Dornhorst, A. C. *Ibid*, 1955, i, 1185.
7. Auchincloss, J. H., Cook, E., Renzetti, A. *J. clin. Invest.* 1955, **34**, 1537.
8. Fishman, A. P., Samet, P., Cournand, A. *Amer. J. Med.* 1955, **19**, 533.
9. Galdston, M. *Ibid*, p. 516.
10. Counihan, T. B., Evans, E. M., Milne, M. D. *Clin. Sci.* 1954, **13**, 583.
11. Rapoport, S., Guest, G. M. *J. clin. Invest.* 1945, **24**, 759.
12. Wégria, R., Capeci, N., Kiss, G., Glaviano, V., Keating, J., Hilton, J. *Amer. J. Med.* 1955, **19**, 509.
13. Tenney, S. M., Miller, R. M. *Ibid*, p. 495.

## TREATMENT OF HYPERTROPHIC PYLORIC STENOSIS

IT has been estimated [1] that hypertrophic pyloric stenosis appears in 3 or 4 out of every 1000 newborn infants. The mortality of the condition has fallen strikingly in the past thirty years, partly because of the general reduction in infant mortality but mainly because of better diagnosis and treatment. Surgical treatment is now more or less confined to Rammstedt's operation of pylorotomy, which has superseded earlier procedures such as gastro-enterostomy or forcible dilatation of the pylorus. Medical treatment consists of stomach washouts, careful graduated feeding, and the administration of a spasmolytic drug of the atropine series. Atropine itself has been largely replaced by methyl atropine nitrate, which has a greater cholinergic effect, and this drug, either in watery or alcoholic solution, or in the form of lamellæ given sublingually, has been the standard drug. A new spasmolytic derived from scopolamine has now been used in a clinical trial described by Corner,[2] following favourable reports from Scandinavia.[3] Methyl scopolamine nitrate is said to have five times the spasmolytic effect of atropine on guineapig intestine and two to three times that of methyl atropine nitrate. Further, in ordinary doses, it less often has such side-effects as dryness of the mouth and mydriasis.

Corner treated 117 babies with the new drug, combined with a strict feeding plan and the administration of parenteral fluids when necessary. The diagnosis was established by two criteria—visible gastric peristalsis and a palpable pyloric tumour—and confirmed by two experienced observers. All cases were treated in hospital and the earlier ones were kept in hospital for the whole period of treatment. The drug was generally given by mouth in doses of 0·1 mg. six times daily, fifteen minutes before feeds. If vomiting recurred, or the child was severely dehydrated at the start of treatment, the drug was given subcutaneously in doses of 0·05 mg. six times daily. At the beginning of the trial supplies of the drug were scarce and treatment had to be stopped after a few weeks, and this sometimes led to relapse. Later on, however, it was possible to continue treatment for at least ten weeks and relapses no longer occurred. The response to treatment was usually very rapid, vomiting ceasing immediately in 75 cases and within forty-eight hours in a further 19. A few infants continued to vomit slightly even after five days, but their condition was otherwise satisfactory and treatment was continued. Gain in weight was at first rather slow in many babies, but this could be partly attributed to the low calorie intake at the start of treatment. One child died during the course of treatment: he was severely infected and although vomiting was controlled he had persistent anorexia and died after four weeks' treatment. Another child responded inadequately to treatment, and Rammstedt's operation was performed on the nineteenth day.

This trial confirms previous reports of the effectiveness of the drug in hypertrophic pyloric stenosis. It does not, however, decisively settle the argument in favour of medical treatment on the one hand or surgery on the other. In the best circumstances, the mortality from surgery is now very low [4 5]; and the big advantage of operation is that the infant can be sent home after a few days on a normal feed and no further supervision is usually needed once the sutures are removed. Recurrence after operation is exceptional. Medical treatment, on the other hand, requires a long period of supervision, with frequent visits to hospital. Drug treatment must be continued for many weeks, and if for some reason the

1. Davison, G. *Arch. Dis. Childh.* 1946, **21**, 113.
2. Corner, B. D. *Ibid*, 1955, **30**, 377.
3. Malmberg, N. *Acta pædiatr., Stockh.* 1949, **38**, 472.
4. Wood, E. C., Smellie, J. M. *Lancet*, 1951, ii, 3.
5. Browne, D. *Proc. R. Soc. Med.* 1951, **44**, 1057.

mother stops treatment the symptoms are liable to recur. Further, the lengthy treatment may lead to an over-protective attitude by the mother and breed difficulties in later life. Surgical success depends on the skill and experience of the surgeon and the quality of the nursing care. Rammstedt's operation seems deceptively simple in expert hands, but requires constant practice for good results. Todd [6] suggested that the indications for operation were failure of medical treatment after a trial of seven days, gross dehydration, and a birth-weight below 7 lb. But if an experienced surgeon is available, operation is probably the best treatment unless there is severe infection.

## CHEMOTHERAPY OF TUBERCULOSIS

A REPORT of the 14th conference on tuberculosis chemotherapy of the Veterans Administration and National Tuberculosis Association of the U.S.A. has lately appeared.[7] It is nine years since the 1st conference was held, when the early results of treatment with streptomycin at nine Veterans Administration hospitals were described. The list of transactions at the 14th conference clearly reflects the great advance in our knowledge of antituberculous drugs, as well as the value of continuous coöperation in studying them. Streptomycin, *p*-aminosalicylic acid, and isoniazid in various combinations occupy much of the story; but there is also news of pyrazinamide, cycloserine, tetracycline, viomycin, s-ethyl-*l*-cysteine, streptohydrazide, calcium benzoyl *p*-aminosalicylate, corticotrophin, and D-glucuronolactone isonicotinyl hydrazide. The experimental design of the American organisations' large-scale trials may not always be perfect; but a machine has been constructed and maintained capable of giving valuable information in a short time and flexible enough to adapt itself rapidly to changing ideas. The Medical Research Council's trials in this country are more rigorous and precise: they ask fewer questions, and the answers are correspondingly more definite. The two types of coöperative clinical research are complementary to each other.

The future programme of the Veterans Administration includes a study of the surgical removal of lesions remaining after antibacterial treatment. As we observed recently,[8] only a controlled trial will finally decide whether it is necessary to remove such lesions. Such a trial was started in a Veterans Administration hospital in June, 1953.[9] By the end of 1954, 59 patients had been allocated at random to resection and non-resection groups. So far 2 of the 33 who had a resection and 2 of the 26 who did not have shown bacteriological or radiographic evidence of relapse. But it is much too early to draw conclusions. The clinical trials of the U.S. Public Health Service also include examination of another important problem. A random group of children with uncomplicated primary tuberculosis is being treated for a year with isoniazid while a similar group receives inert tablets. The children will be followed for two years and it is hoped, if sufficient numbers can be included in the trial, to find out whether isoniazid does indeed reduce the incidence of complications.[10] Bentley [11] has lately expressed concern lest chemotherapy should actually increase the incidence of segmental lesions in the lungs of these children. In this country the M.R.C. are planning a trial of long-continued antibacterial treatment of chronic infectious patients [12]—another important aspect of modern therapy.

There remains the question of using isoniazid alone in pulmonary tuberculosis.[13] Here again, the Veterans Administration are carrying out a pilot study. Unfortunately, no doubt for ethical reasons, only patients without lung cavities will be treated, and the trial is unlikely to give a clear-cut answer to the main problem. In this country too such a trial would hardly be acceptable [11]; but it could perhaps be carried out in countries where the social conditions justify taking a known risk for the sake of providing the only feasible treatment for large numbers of tuberculous patients.

6. Todd, R. McL. *Arch. Dis. Childh.* 1947, **22**, 75.
7. Transactions of 14th Conference on the Chemotherapy of Tuberculosis. Veterans Administration. Washington, U.S.A. February, 1955.
8. *Lancet*, Aug. 13, 1955, p. 330.
9. Raleigh, J. W., Decker, A. M., Bell, J. W. Trans. 14th Conf. Chemotherapy of Tuberculosis, 1955, p. 199.
10. Ferebee, S. H. *Ibid*, p. 123.
11. Bentley, F. J. *Brit. med. J.* Oct. 29, 1955, p. 1084.
12. D'Arcy Hart, P. *Lancet*, Sept. 3, 1955, p. 509.
13. *Ibid*, 1955, i, 238.

## ANOTHER NEW BLOOD-GROUP

MANY new blood-groups have been discovered because an antibody has appeared in the blood of a patient who has been repeatedly transfused. Recently a hitherto unidentified antibody was detected in the serum of a Mr. V when his blood was being cross-matched for his 27th transfusion; and details of this antibody, named after him, have been reported from New York and London by DeNatale, Cahan, Jack, Race, and Sanger.[14] Mr. V was in St. Luke's Hospital, New York City, and the prospective donor was a Negro. Inquiry showed that 6 previous donors had been Negroes, and tests with a set of 20 standard test cells showed that the only positive reactions with Mr. V's antibody were obtained with 2 of the 6 specimens of Negro blood that happened to be included in the standard set. Attention was thus directed to Negro blood, and samples from 168 New York Negroes were tested; 45 (27%) reacted positively with the V antibody. The blood of 444 white blood-donors was tested and only 2 (0·5%) positive samples were found; both were natives of Puerto Rico. Investigations were extended to London and to West Africa. In London 407 samples of blood were tested and only 2 (0·5%) V-positive reactors were found; but a group of 150 West Africans living in Lagos or Accra included 60 (40%) V-positive reactors. When the rest of the blood-groups of the tested bloods were worked out, it was seen that V-positive is particularly associated with the Rh types cde and cDe. For this reason it is thought that the V antigen is somehow connected with the Rh blood-group system, but at present the precise connection is unknown.

Racial differences in the distribution of blood-groups are well known, and Mourant [15] has shown how much information has been accumulated. There are other examples of gross racial differences. Thus only 3% of Chinese are Rh (cde) negative, and the cde chromosome is rare or entirely absent in the Siamese and in Central American natives. The North American Indians show only groups O and A, with a remarkable preponderance of group O; the distribution in the Chippewa Indians is 87·5% group O and 12·5% group A, with none in groups B or AB. It is already known that African Negroes (south of the Sahara) show a high frequency of cDe; various races show from 48 to 90%, with an average of 60%, and the mutation cD$^{u}$e is almost limited to these peoples.

From a practical point of view we need to know whether the V antigen is likely to lead to the formation of antibodies, and whether consequently Negro donors should be avoided when taking blood for transfusion into white recipients. Fortunately, V is apparently not a powerful immuniser. As DeNatale et al. point out, "tens of thousands of white people must have received blood transfused from Negro donors, yet only Mr. V has responded by making anti-V." The antibody will be found, and any possible reaction will occur, only after a second transfusion of Negro blood. Blood from the two V-positive English donors was found to be still surviving in their V-negative recipients two or three weeks after transfusion. Nor is it thought that the V antigen is likely to cause hæmolytic disease in newborn Negro infants,

14. DeNatale, A., Cahan, A., Jack, J. A., Race, R. R., Sanger, R. *J. Amer. med. Ass.* 1955, **159**, 247.
15. Mourant, A. E. The Distribution of the Human Blood Groups. Oxford, 1954.

because 20% of Negro matings would provide babies in which incompatibility of this type would arise, yet the disease is relatively uncommon, and when it does occur it can usually be traced to Rh (anti-D) incompatibility.

No doubt transfusion centres will now include V-positive Negro cells among their test groups, but the rest of us can breathe a sigh of relief on learning that this new group is not one that needs to be reckoned with in everyday blood-transfusion work.

## TOXIC INSECTICIDES

CHEMICAL insecticides have saved millions from malaria, typhus, plague, dysentery, and other insect-borne diseases, and they have greatly increased the world's food production. But many of them are toxic to man and other mammals. The organic phosphorus compounds are especially dangerous because they inhibit the cholinesterases of the blood and nervous system. Symptoms of poisoning are therefore due to failure of transmission of nerve impulses at synapses in the central nervous system and peripheral ganglia and at the motor end-plates of voluntary muscles. The chlorinated hydrocarbons form another group of chemical insecticides, of which dicophane (D.D.T., chlorophenothane), gammabenzene hexachloride (B.H.C., 'Gammexane'), aldrin and dieldrin, chlordane, heptachlor, methoxychlor, and toxaphene (chlorinated camphene) are the best known. They have certain properties in common: they are soluble in fats and common organic solvents and insoluble in water; and all are relatively stable compounds. They are stored in the fat depots of man and warm-blooded animals. Acute poisoning results in disturbances of the central nervous system, and excitement, tremors, spastic and flaccid paralysis, and convulsions follow the absorption of large doses. Six years ago,[1] we said that dicophane and gammabenzene hexachloride seemed to be the safest insecticides under normal conditions of pest control by experts, but that the cumulative effects of small doses had not been fully established. This statement is still true today.

Many symptoms have been ascribed to chronic dicophane poisoning. Case[2] found that Servicemen exposed to high concentrations were liable to fatigue, emotional instability, and violent cramps in the limbs. Campbell[3] described similar symptoms in a man who had been demonstrating the use of dicophane for six years. Later Campbell[4] recorded 5 cases of peripheral neuritis (1 patient had a retrobulbar neuritis) and 2 other cases of isolated retrobulbar neuritis. All these patients had been using a proprietary insecticide containing dicophane and pentachlorophenol for treating woodworm; so it was not certain that these symptoms were entirely due to dicophane. Peripheral neuritis with purpura was also noted[4] in a chemist preparing a dicophane aerosol. In 5 children under three who were exposed to dicophane, purpura developed; 4 were found to have thrombocytopenia and 2 had symptoms of nervous involvement (convulsions and loss of coördination).[5] A case of fatal aplastic anæmia with thrombocytopenic purpura was reported in the United States.[6]

The greatest danger to the general population could arise from the constant ingestion of small amounts of dicophane sprayed on fruit and vegetables or contained in the fat of animals eaten as meat. Occasionally large doses have been accidentally taken by mouth: once dicophane-concentrate powder was mistaken for baking-powder[7] and as much as 120 mg. per kg. body-weight was absorbed in one dose (7 out of a family of 11 were affected but all recovered). But men exposed to varying concentrations of dicophane every day in their work failed to show any abnormalities.[8] Princi[9] holds that no true case of chronic poisoning has ever resulted from exposure to any of the chlorinated hydrocarbons.

As insecticide-resistant insects emerge, more potent chemicals are being produced, and they are often brought into general use before their toxic effects on man and domestic animals is known or understood. One of these, chlordane,[10] is regarded as one of the more dangerous of the chlorinated hydrocarbons. It can be absorbed through the intact skin, and little is known about its toxic properties. For these reasons its use on food crops or forage, hay, or silage crops intended as foodstuffs for dairy animals or poultry is prohibited. And, in general, until active insecticides harmless to man have been developed, all these compounds must be handled with great care.

## "MIDDLE-LOBE SYNDROME"

THE middle-lobe bronchus is peculiarly liable to occlusion from extrinsic pressure, because it is comparatively narrow and short, and because lymph-glands are so disposed around it that if they enlarge they will compress it like the jaws of a nutcracker. Moreover, as these glands drain the adjacent lower lobe as well as the middle lobe, atelectasis of the right middle lobe is a fairly common sequel of primary tuberculosis—a fact which was pointed out by Brock et al.[11] as long ago as 1937. Supervening infection may give rise to symptoms soon after the bronchus has been obstructed, and then diagnosis is easy; but quite often there is no trouble for years, and then the occurrence, say, of hæmoptysis, coupled with the radiological picture of a collapsed right middle lobe, has a misleadingly sinister appearance. If lobectomy is performed, enlarged glands may be found compressing the middle-lobe bronchus or they may have shrunk in the course of time and histological examination may show no evidence of specific disease. As some of these patients are tuberculin-negative,[12] it is clear that the original lymphadenopathy is not always tuberculous, but the distinction is of no practical importance. This sequence of events has been described by several workers and it has become widely known as the "middle-lobe syndrome."[12–16]

When respiratory symptoms are shown to have their origin in a diseased right middle lobe, this condition must be borne in mind; but a report on a series of such cases by Lindskog and Spear[17] is a useful reminder that it should not be overemphasised in the differential diagnosis. Some of their cases proved to be examples of the so-called middle-lobe syndrome, but others turned out to be bronchial carcinoma, tuberculosis, abscess following tooth extraction, aspiration lipoid pneumonia, and so on. It would, therefore, be unfortunate if the interest aroused by the middle-lobe syndrome tended to delay adequate investigation of middle-lobe disease; and as there is little justification for the term in any case, it might well be discarded. The condition is merely an area of infected atelectasis resulting from bronchostenosis due to lymphadenopathy; the middle lobe is a common but by no means exclusive site, and as a variety of disease processes may produce the same clinical and radiological picture, each case must be dealt with on its merits.

1. See *Lancet*, 1949, 1, 658.
2. Case, R. A. M. *Brit. med. J.* 1945, ii, 842.
3. Campbell, A. M. G. *Lancet*, 1949, ii, 1178.
4. Campbell, A. M. G. *Brit. med. J.* 1952, ii, 415.
5. Karpinski, F. E. *J. Pædiat.* 1950, **37**, 373.
6. *J. Amer. med. Ass.* 1951, **145**, 728.
7. Hsieh, H. C. *Arch. industr. Hyg.* 1954, **10**, 344.
8. McGee, L. C. *Industr. Med.* 1955, **24**, 101.
9. Princi, F. 11th International Congress of Industrial Medicine, Naples, 1954.
10. *J. Amer. med. Ass.* 1955, **158**, 1364.
11. Brock, R. C., Cann, R. J., Dickinson, J. R. *Guy's Hosp. Rep.* 1937, **17**, 295.
12. Fretheim, B. *Thorax*, 1952, **7**, 156.
13. Graham, E. A., Burford, T. H., Mayer, J. H. *Postgrad. med. J.* 1948, **4**, 29.
14. Paulson, D. L., Shaw, R. R. *J. thorac. Surg.* 1949, **18**, 747.
15. Brock, R. C. *Thorax*, 1950, **5**, 5.
16. Rubin, E. H., Rubin, M. *Dis. Chest*, 1950, **18**, 127.
17. Lindskog, G. E., Spear, H. C. *New Engl. J. Med.* 1955, **253**, 489.

# Special Articles

## THE FIRST THREE YEARS OF A PROVINCIAL PÆDIATRICIAN*

HUGH JOLLY
M.A., M.D. Camb., M.R.C.P., D.C.H.
PÆDIATRICIAN, PLYMOUTH CLINICAL AREA

JUST over three years ago I became a consultant pædiatrician in the provinces after spending my registrar period in London. During this time I have become concerned at the width of the gulf between London and provincial pædiatrics, and particularly at the fact that the average pædiatric registrar does not learn enough of the sort of work he would meet as a provincial consultant. Because of this I have been encouraged to present a critical analysis of my first years in the provinces. My remarks refer to London because I have no experience of the other large centres, but their problems must be similar in some respects.

This is the first consultant pædiatric appointment to be held in Plymouth, and the clinical area covered stretches across to Bude on the north coast of Cornwall, down half-way to Truro, and up half-way to Exeter. Geographically we are more fortunate than many areas because, though the total population is 350,000, 220,000 live in Plymouth, and this is the natural focal point of the area. Our distance from London and other main centres makes us largely independent.

All the beds for which I am directly responsible are in one hospital. They consist of a premature-baby unit and neonatal beds, a ward for children over 18 months, and a new cubicle unit for babies shown in the photograph. When I first came I had a share of two house-physicians, but there is now a house-physician and a registrar for the department.

### CONTACT WITH COLLEAGUES

One of my earliest and most pleasant surprises was the close liaison possible with the general practitioners, as compared with London. I felt that the standard of general practice was higher than in London, at any rate as seen through the eyes of a pædiatric registrar. I was particularly impressed by the high standard of the doctors' letters which accompanied the patients.

This close personal contact with practitioners exists because we meet often, both socially and professionally—especially during domiciliary visits, a service of which much fuller use is made in the provinces. Practitioners also attend ward rounds and outpatients from time to time, and occasionally they still accompany their patients to the consultation, particularly in the peripheral clinics in the country. Another form of contact is through lecturing to medical societies, and I have now addressed several of the groups in the area. From time to time I am asked to attend doctors' children, and during the winter I find that my work as a "general practitioner" for these children is quite considerable. Again, an evening rarely passes without at least one telephone call from a doctor who wishes to discuss a case without my necessarily being asked to see the child. My impression is that these personal calls are much commoner than in London, and they give endless opportunities for discussion of modern pædiatric methods with the family doctor, as well as for receiving his suggestions. One of the results of this close association is that it is possible to discharge children from hospital for home nursing much earlier than one could in London.

Despite all this I would like to attain a still closer relation with the practitioner, especially over the admission of patients. We have a bed bureau, comparable to the Emergency Bed Service in London, but I have always felt this to be a very impersonal method. It is obviously a necessary evil in London, but less so with us and I am doing what I can to encourage practitioners to phone one of the pædiatric staff instead, since we learn far more about the child from a phone call than from any letter. The practitioner's complaint that he wastes time while the telephonist finds the house-physician has been largely met by a modern call-system.

A second important liaison is with the public-health departments of Plymouth, Devon County, and Cornwall County, from whom I have had unlimited coöperation. When I arrived I found that children were being referred to outpatients by school and infant-welfare officers without reference to the family doctor. This was obviously undesirable, especially as the child was sometimes later referred to outpatients by the family doctor. It was therefore agreed that all clinic cases requiring a pædiatric opinion would be referred to their family doctor in the first instance. As a corollary I arranged that copies of my outpatient and discharge-letters should be sent to the medical officer of health for distribution to the clinic concerned with the child. Only two practitioners raised any objection to this and once it was pointed out that it was only fair since the clinics were no longer referring the patients direct, the objection was withdrawn.

The M.O.H. for Plymouth has arranged for each of his health visitors to attend my outpatients for three months, and this is a tremendous help to me. These nurses often arrive armed with a great deal of information about a child due to attend, which they have been given by the health

View of the new cubicle unit for babies.

* Read before the British Pædiatric Association in April, 1955.

visitor in charge of the case. The outpatient health visitor takes notes on the children who attend and passes on this information to their own health visitor when she meets them all on the morning after outpatients. It is therefore easy for me to refer any requests about a child to the health visitor concerned and to pass on any new ideas on pædiatrics in general. Unfortunately, owing to the shortage of health visitors in Plymouth they do not yet work in the pædiatric or maternity wards, but this is to be remedied as soon as the numbers increase. At the same time, the atmosphere in the wards is such that they are very welcome there, and they often call to see a child in whom they are interested. The health visitors tell me that, now they are more closely associated with the hospital, their status has risen in the eyes both of the family doctor and the parent.

The M.O.H. has helped in countless other ways. In my first year I found that in Plymouth there was a surprisingly high incidence of ferrous-sulphate and lead poisoning. The M.O.H. agreed to send a circular to this effect to all practitioners and chemists, which led to a dramatic fall in both conditions.

Close association has also been possible with the tuberculosis staff and with other branches of the public-health department. I now hold a study day twice a year for these medical officers and some of them are attached as clinical assistants to the outpatient department.

### OPPORTUNITIES FOR TEACHING AND LEARNING

In moving deep into the provinces I have felt the greatest losses to be the reduction in academic atmosphere, and the lack of student-teaching. Nothing can make up for these, but an unexpected compensation has been the greater opportunity for combined clinical work with consultants in other specialties.

For the surgical aspect of my own patients I work mainly with one surgeon. We do our outpatients and rounds on the same days and can therefore achieve a high degree of collaboration. This surgeon is now a member of the British Association of Pædiatric Surgeons and of our own South-West Pædiatric Club. I also have a weekly round with two other surgeons on their patients in the children's ward of another hospital and a weekly upper-respiratory clinic with an E.N.T. surgeon and an oral surgeon. Once a month I attend a general orthopædic clinic with one orthopædic surgeon and once a month with another orthopædic surgeon I attend a clinic for cerebral palsy. I do a screening session with a radiologist once a week, while my rounds of the neonatal beds are undertaken with the obstetric house staff so as to coöperate closely with the two obstetricians.

In the south-west region we are fortunate in having a professor of child health in Bristol who takes a fatherly interest in each of the clinical areas, and this is immensely to our advantage. We are known to have central support for our development schemes, and in Plymouth an obvious advantage has been the creation of a pædiatric registrarship shared with Bristol. The registrar spends one year in Bristol Children's Hospital and one year in Plymouth.

Most people agree that this interchange of registrars between teaching hospital and provincial centre is desirable, yet it is still rare. For the registrar, provincial experience is invaluable, if only because he will learn at first hand the work of a provincial consultant, which is the type of work he may ultimately undertake himself. He will see more of the possibilities for preventive pædiatrics than in London and he will have greater responsibilities, while the clinical material from so large an area is almost limitless. The amount of experience with the newborn is greater than in many teaching centres, and a premature-baby unit with a yearly admission-rate of 250 babies offers endless possibilities. The job demands more tact because of the closer relationship with the family doctor, but a good registrar will find that he is often phoned by the family doctor for advice. In this region we have started a form of specialist consultant service between ourselves. For example, a pædiatrician and a radiologist have visited centres to see groups of children with cardiac conditions and I have seen some with endocrine disorders.

I feel that there is room for more visits to the provinces from physicians and surgeons in the main centres. We are lucky in being in a holiday area and each summer lay nets across the main roads to trap and entice to Plymouth any visiting pædiatricians. As we are also the closest port to America and on the fastest route from the States to London, a number of American pædiatricians have visited us. Interestingly enough, I find that American pædiatricians are amazed at the possibilities available in an English provincial centre as compared with their own.

Lately a surgeon from London has operated here on two cases of hydrocephalus using a new technique he has designed. Demonstrations of this kind in the provinces would increase the amount of work which can be done there. For some time we have been working on hydrocephalus [1] and this experience has convinced me that greater use should be made of provincial centres for specialised research, since the closer association possible between physician and surgeon makes them particularly suited to this type of work. Our own research involves five consultants, but we have never had any real difficulty in getting everybody together. In the area we also have one of the few residential schools for cerebral palsy, and the four consultants involved make use of this centre for research as well as for therapy.

I should like to see these exchanges extended to include students, whether undergraduate or postgraduate. Edinburgh has a scheme whereby its medical students have to attend some other centre during their summer vacation, and in Plymouth we thoroughly enjoy these visits. The students are attached to different departments and can gain an immense amount of experience and teaching from consultants who miss the opportunity for teaching in the normal run and are glad to do it. I would welcome groups of say 4–6 students at any time and would guarantee to make their stay worth while. As for postgraduates, my own feeling is that those attending courses at Great Ormond Street are not learning enough of the general-practitioner pædiatrics required by those who do not aim at becoming consultants. This is more easily taught in provincial centres and I believe that these postgraduates should spend half their time in the provinces and half in London.

One of Plymouth's greatest disadvantages is its distance from London; but the length of this distance is to some extent an attitude of mind! Since moving to the West I have maintained that Plymouth is a suburb of London, and now that I have taken to driving up after dinner this has become more true. One must attend meetings in London and other large centres, and every opportunity should be given to provincial consultants to attend courses in London. The provincial consultant is often readier to travel than his London colleague, and I am always interested to see the number who have come long distances for London meetings.

The other major disadvantage is the isolation from pædiatric colleagues. This is hard to overcome, but my nearest pædiatric colleague, who is in Exeter, and I hold a round in each other's hospital one Saturday in every month. In the ideal pædiatric service of the future every centre would be big enough to have at least two pædiatricians on its staff. A further criticism of the present organisation is that in many areas the pædiatrician

1. Jolly, H. R. *Proc. R. Soc. Med.* 1955. 48, 843.

still has no entry to the fever hospital and no facilities for the treatment of gastro-enteritis.

From my own experience I would suggest to the newly appointed provincial pædiatrician that his first task should be to start a premature-baby unit if none exists, because that is the quickest way to save lives. Since our unit started, the neonatal-mortality rate for premature babies in Plymouth has fallen from 203 to 169. We are fortunate in having an additional sister who looks after suitable premature babies on the district. This nurse is on the staff of the M.O.H. but attends ward rounds in the unit and is very much part of the department. She also takes on feeding problems in full-term newborn babies if her time permits.

I would also advise the new consultant to concentrate his work in one hospital at the centre and not to undertake peripheral work until his base is secure.

Summing up the advantages of provincial pædiatrics I should say that the greatest of these was the chance to practise child health in a manner which is impossible in London. (Much of this conception we owe, of course, to Spence's work in Newcastle.) I believe that the pædiatrician has a greater opportunity than any other consultant to serve a community, and that the way to achieve this is to work through the doctors in that community. Moreover, he has the opportunity to inspire with modern pædiatric ideas not only the doctors but also the nurses. In the provinces the consultant has more beds and often more varied clinical material because of the size of the area drained, and, despite the distances, he probably spends less time in travelling than his colleagues in London, for he can move faster as well as more pleasantly.

He can keep in touch more easily with his interesting patients, not by unnecessary outpatient-attendance but by inquiry from the child's own doctor when they meet. Also, he can usually be certain that a child who falls ill again will be sent back to his unit and not to some other hospital.

In view of all this I feel that, whatever his particular interests, every young pædiatrician should spend at least five years in the provinces as an essential part of his training.

## INFANTS IN MATERNITY UNITS

A MEMORANDUM[1] from the Ministry of Health to regional hospital boards, hospital management committees, and boards of governors suggests methods for the improvement of existing arrangements for the care of infants in maternity units.

The memorandum points out that, for the most part, infants in maternity units are kept either in nurseries or in lying-in wards with their mothers. The congregation of a large number of infants in a nursery is not without danger, principally from the spread of infection and less commonly from accidents. The Ministry is particularly uneasy about the practice of leaving a number of newborn babies alone in a nursery, especially at night, except for periodic visits by a nurse who, in the course of other duties, pays occasional visits to the nursery. Occasionally a baby has been found dead in his cot, death perhaps having been caused by suffocation or by inhalation of regurgitated food. Such deaths are fortunately rare—9 deaths during the first fourteen days of life occurred from this cause in hospitals in 1952 and 16 in 1953. Infants who die in this way may in fact have been ailing—though almost "silently" so—for a few hours before death. These deaths should be less likely when the infants are under constant supervision by the mothers or the nursing staff, who may detect any slight deviation from the normal.

The practice of keeping babies with their mothers, generally known as "rooming-in," either continuously or for the greater part of the time has certain advantages, the memorandum continues. The mother gets to know her baby and learns how to care for him: the mother-child relationship is gradually and steadily established. Where the mother and baby are in a single room the risk of infection is reduced to a minimum and even in larger wards the risk of an epidemic spreading to all infants is reduced. The infants are not subjected to frequent changes of environment and temperature by being taken at intervals to and from nursery and lying-in ward for feeding. As the infant is constantly under the eye of the mother and nursing staff, any abnormal sign is likely to attract attention at once. Where it is at all possible, the infant should remain in the ward with the mother. Where for any reason this is inadvisable—for example, when the infant is noisy and troublesome or when the mother is not well—the infant should be kept in a nursery until it is possible to return him to his mother with no disturbing results.

Where infants must be kept in a nursery, the number should be small. There should always be adequate cot spacing so as to decrease the chances of cross-infection, and the nursery should be near the lying-in ward so that infants may be easily taken to their mothers for feeding and nursing. Where possible a member of the staff should be in constant attendance.

The memorandum says that "rooming-in" should not normally require any extension or adaptation of premises; some reallocation of existing accommodation is likely to be sufficient in most cases. This practice should, however, be borne in mind when new maternity units are being planned.

1. H.M. (55)116.

## DRUGS AND BEDS

IN their third report[1] in the 1955–56 session the Committee of Public Accounts give further particulars of the Ministry of Health's investigations into the prices of standard drugs, proprietary preparations, and basic drugs. The prices paid for standard drugs, they were glad to learn, had on the whole not been excessive. But the profits on some of the 91 proprietary preparations selected for investigation reached 60% on selling prices, and the return on capital, when it could be calculated, ranged from a loss of 24% to a profit of over 100%. Three of the firms, the committee were glad to learn, had lately made price reductions which would save the Exchequer about £850,000 a year. The investigation into basic drugs covered four selected groups on which N.H.S. annual expenditure was about £10 million. Here, too, trading results varied. Some firms seemed to have made losses, but some of the larger suppliers of antibiotics appeared to have made profits of 30–40% on selling prices.

To the committee these findings were unsatisfactory and they were concerned at the continued payment of prices which seemed to allow "a profit margin substantially in excess of that hitherto accepted as appropriate for Government contracts." Their concern was not lessened by the evidence of the Ministry and the Treasury that little progress had been made in negotiating with the industry. Drugs provided under the N.H.S. were supplied by retail chemists from stocks and not bought direct by the Government, and the committee recognised that this practice made it difficult to fix a suitable price. They suggested, therefore, that manufacturers whose prices had been shown by costing to be excessive might be persuaded to give annual rebates to the N.H.S.

The committee counted the cost from the doctor's as well as the chemist's point of view. In 1954–55 some 244 million prescriptions were dispensed under the N.H.S.

1. H.M. Stationery Office, 1955. Pp. 21. 1s.

In 1949 the average cost per prescription in England and Wales was 3*s*. 1*d*.; in August, 1954, it was 4*s*. 4*d*., and more lately in Scotland it was 5*s*. 2*d*. The increase was mainly due to new expensive drugs, but a secondary cause was an increase in the proportion of proprietary preparations prescribed, many of which cost more than their equivalent standard drugs. The committee appreciated that under the N.H.S. a doctor had an absolute right to prescribe what he considered medically suitable for his patient, but they also recognised that the taxpayer had "every right to expect due economy in prescribing."

HOSPITAL PROBLEMS

Variations in the costs of different hospitals also attracted the committee's attention. They appreciated that the variation in the range of services provided in different hospitals was necessarily reflected in the cost of running the hospital. Uniformity was not to be expected. But a study of the costing returns of other hospitals could offer useful pointers, and the regional hospital boards had made substantial economies based on investigations into differences of expenditure. The board of governors of teaching hospitals had not been so coöperative. Of the 34 boards of governors, 17 indicated that the returns were of little or no use to them, 5 made no reply. The committee were particularly surprised to learn that the board of governors of St. Bartholomew's Hospital had not found these comparisons of cost worth consideration, for the cost per patient a week at Barts was £28 9*s*. 9*d*., compared with an average of £25 4*s*. 2*d*. for all general teaching hospitals in London, and the cost of provisions in 1953–54 was 8*s*. per patient week more than at any other London teaching hospital.

Another group of teaching hospitals, the United Manchester Hospitals, also drew the committee's fire. Year after year, they pointed out, the auditors have met with a refusal on the part of the board to interfere with the policy of their own management committees by insisting on group-purchasing of provisions and competitive tendering. The board contended that the hospitals had had good and long service from their present suppliers and that bulk-purchasing would bring only small economies. But the committee remained unconvinced that independent purchasing by each hospital of commodities in common demand was as economical as joint-purchasing for the whole group.

## Points of View

### DO WE REALLY NEED MORE HOSPITAL BEDS?

SOMERVILLE HASTINGS
M.S. Lond., F.R.C.S., M.P.

THE incidence of disease is changing with almost alarming rapidity. Infectious disease is decreasing rapidly, partly because we are now able to prevent and treat it more efficiently but mainly perhaps because overcrowding is much less. The death-rate from tuberculosis is falling although the incidence is still high. Some believe that if we once decided to treat tuberculosis as an infectious disease it might be eliminated within a generation. Children's wards and children's hospitals are being closed or taken over for adults, because of the rising standard of life, less overcrowding, the provision of milk in schools, as well as a safer milk-supply as the result of pasteurisation or tuberculin-tested herds.

On the other hand the incidence of psychosomatic disease seems to be extending. But whether there is a true increase or merely an increasing recognition of a psychological element in a greater number of diseases it is difficult to say. Undoubtedly there are many more old people, and these are more prone to sickness than normal healthy adults. They do, however, recover as a rule, though less rapidly than younger people.

To what extent can we foresee the future incidence of disease and model our hospital policy accordingly? In Basildon, Harlow, and other new towns they are building factories that are at first mere shells but can be divided up according to the industry that is developed in them. Is there a lesson here for hospital development?

Our principal voluntary hospitals, and especially our teaching hospitals, developed in response to an urgent national need. The Industrial Revolution resulted in overcrowding and appalling conditions of life. The homes of the people were too bad to be ill in, or even to die in, and something had to be done. Because the voluntary hospitals were incapable of fully supplying the need the poor-law infirmaries were called in and had to assist in the good work.

But housing conditions are improving and an increasing number of people live in houses with 2 or 3 bedrooms in which it is possible to be ill in relative comfort, provided of course that medical and nursing services are available and no surgical or other specialised treatment is required. Moreover, there is increasing evidence that certain classes of people do much better at home under such conditions. This applies especially to children and old people. It seems clear that the psychological effect of removal to hospital affects adversely some children. Old people also move badly and in many cases do not survive for more than a week or two. The reason for this is by no means clear. It may be in part psychological, since in the bad old days few old people ever returned to their homes from poor-law infirmaries. Some chest physicians are treating many more cases of pulmonary tuberculosis at home. They claim that for psychological and other reasons they often do much better.

There can be no doubt that many more hospital beds for mentally deficient children are required. There can be no doubt, too, that many hospital wards, indeed whole hospitals, are hopelessly out of date and lacking in essential facilities. One has only to visit modern hospitals, such as those recently built in Basle and Zürich, to realise how great is our need. In the new general hospital at Zürich the largest ward has 6 beds only.

What we urgently require is better hospitals, But do we actually require more beds? And if these were provided could we staff them? Today there are thousands of hospital beds in buildings of moderate quality empty for want of staff. Are not half-way houses for old people, in which hospital facilities can be brought to the patients as and when required, a much greater need? In the vast majority of illnesses in old people, medical and nursing care can be given in such accommodation without removing the patient.

It is easy to understand why doctors should ask for more hospitals, especially in the areas where they are practising. It is much easier to do good work if your patient is subject to the discipline of a hospital ward and under the skilled observation of a trained nurse or sister. It is easy to appreciate why every town of any size that has not a general hospital is now demanding one. Bringing hospital facilities to the patient in his home usually implies an increase in the local rates, since these facilities are provided by the local authority and not by the hospital service. Besides it is much nicer to be ill in a hospital near one's home where one's friends can visit daily. More women are now going out to work and have therefore but little time to attend to sickness in the home.

In the case of new towns and large housing estates the demand is especially vociferous. It is pointed out that

in many cases there is no hospital within several miles and that this hospital has already a considerable waiting-list.

But is the best way of meeting this need the building of a series of new and relatively small general hospitals? A small hospital is often neither efficient nor economical to run. Nor should every hospital expect to have inpatient facilities for every specialty. Hospitals can be grouped for this purpose so that, for instance, inpatient treatment for eye or skin diseases can be provided only by one hospital in a group of three or four, and for the rarer specialties such as brain and chest surgery the groups should be much larger. Transport is much easier than it was and it is always possible to provide free transport for patients' friends, if required.

Might not the best solution of these admitted difficulties be found in the provision, in the new towns and elsewhere, of consultative stations for outpatients making specialist advice readily available to the local doctors for their patients, and in linking these stations with parent hospitals to which the consultant is attached, so that continuity by the same specialist can be assured if the patient has to go to hospital for further observation or treatment. This may, of course, imply extension of existing hospitals; but this is infinitely better than building a number of small general hospitals remote from the places of residence of the consultants who are responsible for the patients in them.

Such consultation stations might be in health centres, where they exist, or be built as a first instalment of future health centres. Alternatively, special buildings might be erected or existing buildings adapted. Perhaps best of all, in view of the fact that so many health questions are still in the melting-pot, temporary buildings might be provided, or, as has been so successfully done with health centres at Harlow New Town,[1] buildings might be erected which could be readily converted into ordinary dwelling-houses in case of need.

We certainly need better and more up-to-date hospitals, but do we need to increase the total number of hospital beds?

## Medicine and the Law

### An Overheated Cot

AT an inquest on Nov. 29, the overheating of a cot in a maternity unit was held to be a contributory cause of the death of a three-day-old infant.[2] His mother had toxæmia of pregnancy, and the baby was prematurely delivered by cæsarean section on Nov. 18. He weighed 4 lb. 8 oz. at birth. In evidence, a sister said that she changed the infant to a rack cot on the evening of Nov. 19, and found everything normal, but next morning she and the superintendent sister noticed that the cot thermometer registered 110°F, and that the red warning light (which was under the cot) was burning. The infant's temperature was 105°F. Two pupil midwives who were on duty at times before the warning light was seen said that they had noticed nothing out of the ordinary, and they had not touched the heating switches. The matron of the hospital said that ward sisters were in charge of cot heating and nurses were not allowed to touch the switches. She said that occasionally cots were heated before being occupied by newborn babies, but the switches were not supposed to be left at "high."

A pathologist said that death was due to bilateral adrenal hæmorrhage and atelectasis, prematurity being a contributory factor. He considered that the infant would probably have died in any case, but that the overheating, had it been present for a long period, might have hastened death. A verdict of accidental death was returned.

1. See *Lancet*, Oct. 22, 1955, p. 863.
2. *Staffordshire Evening Sentinel*, Nov. 29, 1955.

## In England Now

*A Running Commentary by Peripatetic Correspondents*

DURING a dull operating-list, my anæsthetist suddenly said she had had a vivid dream about me the previous night. As my anæsthetist was a very attractive young woman, I felt duly flattered. However, it transpired that she had seen me in a plane which crashed and did a double somersault. As each month I fly to a remote hospital and I was due to go the following day, I was able to point out to Betty the implications of her dream. The poor girl was horrified, having forgotten my usual routine visit, but she hastened to add that the dream could not really apply as she had seen me in the pilot's seat. However, it so happened that on this occasion I had not been able to book my usual flight. Instead I was told to contact a certain Captain Evans at 6 A.M. on arrival at the airport. Next morning found me in the cold, grey dawn inquiring for the said gentleman. I ran him to earth in a distant hangar—a striking figure complete with traditional handlebar moustache, rows of ribbons on a faded R.A.F. tunic, and shabby corduroy trousers. He informed me he had only just taken over this charter-plane business, but would be delighted to fly me to my destination. He then volunteered that last week his predecessor had "written off" his plane and himself. Also, that he was licensed to carry freight only and he was sure I would not mind signing on as flight-engineer for the trip. Finally, with what I thought was rather misguided humour, he said would I mind paying in advance so that he could leave the money to his widow? I entered the plane, jammed with luggage, and was immediately requested to occupy the only vacant space—the co-pilot's seat.

Happily, we landed safely, and here the story might have rested, but recently I again met my anæsthetist, whom I had not seen for a long time. No, I was not flying to my remote hospital this weekend; no, there was no chance of an emergency visit, as I had another important engagement. In that case, said Betty, she didn't mind telling me. She had again been troubled by a vivid dream of a plane crash—identical with the dream of five years ago, except for the absolute conviction that it was going to happen this weekend. Of course, we laughed over the absurdity of dreams and the notion that they could have any bearing on real life. I still feel this as I gaze through the windows of the airport lounge and reflect on the reason for my being unable to visit my remote hospital this weekend. In half an hour, I board a plane to take me across the Atlantic.

* * *

We have always been assured that if we kept animals as pets the children would early acquire an understanding of biology. But my faith in the system has been rudely shaken.

We were visited lately by an uncle of mine whom we had not seen for many years: judging by his girth and air of contentment, they had been prosperous years. The children—good hosts as always—were literally all over him. Our three-year-old girl was sitting happily on his knee when there was a pause in the conversation. "Uncle," said she, prodding his abdomen, "are you going to have a baby?" I was not sure of the depth of my uncle's joviality, but I need not have worried. He showed that he was a good psychologist by merely replying "no" with an air of great seriousness. "Well, then," asked the child, "what is it? Is it puppies?"

* * *

Seven years ago I described[1] the pyrotechnic meeting of our dining-club. We are still going strong and this year's meeting was held on Nov. 5 at Stockbridge on the Test. For the first time for many years we had an additional summer meeting at Broadway; and after visiting the Tower and Snowshill Manor some gastronomic explorations took place at a small inn at Ilmington. Regrettably the 15-ton club yacht was sold in 1951. This is a reflection of our increasing commitments and (dare we admit it?) advancing years, and only one member now sails, in a 16 ft. dinghy.

1. *Lancet*, 1948, ii, 787.

Our club is now 30 years old with a record of at least two meetings a year (war years excepted) of which your correspondent has missed one only. But it can, in fact, trace its roots back 35 years, when, as described in the 31st letter of the Corpus (Cambridge) Association, three of its members were in residence at that college—two others being at Emmanuel and Pembroke. These five, together with another, later came to live in Gordon Square, Bloomsbury, whose name the club bears. For longevity as a one-generation club, the Kaleidoscopes of Corpus [2] probably holds the record. This was formed in 1882 by ten Corpus freshmen, eight of whom became parsons, and continued as an annual dining-club, being gradually whittled away by the successive deaths of its members, until the three survivors met sadly to wind it up in 1950 after a life of 68 years.

* * *

Dailys come and dailys go, but ours goes on for ever. She comes up hill, down hill, through wood, through briar, in storm, rain, wind, or snow to reach our little thatched cottage. On arrival she is always cheerful and willing, keeping us permanently amused by her outlook on life. In these democratic days it is embarrassing to be told that there "allus has been gentry and there allus will be," and that she doesn't hold with all this new education and thinks the children would be much better put out to work before they are fifteen, learning something useful.

The eldest of nine, she started work on a dairy farm at the age of twelve and for years went to bed at 5 P.M., because there was nothing else to do. Though her father was earning only ten shillings a week, she has saved throughout her life and now has from £1300 to £1400 tucked away in a savings bank. Her unkempt and unusual appearance suggests gipsy blood, and she has a strange, almost clairvoyant, flair for betting. On Derby Day, listening in together, I found that she had backed the first, second, and third winners all in the right order, but alas, only 1*s.* each way.

Her conversation is limited and repetitive. "It's GOD's truth" follows nearly every statement of hers, and practically all mine are answered by "Well I never." Another of her sayings is "It would be a lovely drying day if it wasn't raining." Nowhere could you find a more honest and affectionate loyalty and I have long ago become accustomed to little idiosyncrasies such as finding my carving knife hidden behind a sofa cushion.

When really ill with bronchitis or flu no power on earth can persuade her to ask her doctor for help, but when she is well or "better than she was," she will walk up two miles to the weekly surgery, dressed in her Sunday best, to ask for a bottle of medicine.

She can turn her hand to anything, from lifting tatties to bottling fruit, and keeping accounts for a butcher. This year she went for the first time in her life more than a few miles from home. This was a coach outing with her Women's Institute to Windsor Castle and she took a most intelligent interest in the whole proceeding. It makes one wonder what "progress" is worth.

* * *

Formerly a strong objector to the Archers as a background to Sunday breakfast, I have lately become an enthusiastic listener, for I find that I pick up a lot of interesting information on agricultural and rural matters from Farmer Dan and his friends. Tom Forrest, for instance, lately described the voracious habits of woodpigeons and offered advice on the habits of the pike. Philip Archer discussed with the vet the differential diagnosis of the sudden sickness which had afflicted his Ayrshire herd. But in the rival programme, Mrs. Dale's Diary, Dr. Dale never warns us on the unwisdom of excessive sunbathing, or gives the pros and cons of isolation for contacts in poliomyelitis. Are we missing an excellent opportunity for health education? Surely much useful information could be impressed on tea-time listeners by the best-known medical household in the country.

* * *

*Heard in committee*

"Mr. Chairman, now that we are frozen to a ceiling . . ."

2. *Camb. Rev.* March 3, 1951.

# Letters to the Editor

## VACANCIES FOR CHEST PHYSICIANS

SIR,—Much has been written about the difficulties of those aspiring to consultant status in the health service. In 1948 the senior hospital medical officer post was created and the various trainee grades were brought into being. The S.H.M.O. grade has been one of the features singled out for most severe criticism, since it has been regarded by many as a form of cheap labour. The numerical strength of this grade in the chest service greatly exceeds that of consultants.

We are employed in the chest service and have become increasingly concerned about the prospects before us and indeed of the general well-being of the service. The following figures show the numbers of consultants and S.H.M.O.s in the chest service by age-groups:

| *Age-group (yr. of birth)* | *England and Wales* | | *Scotland* | | *Total* |
|---|---|---|---|---|---|
| | *Cons.* | *S.H.M.O.s* | *Cons.* | *S.H.M.O.s* | |
| 1880–84 | .. | .. | .. | .. | .. |
| 85–89 | 8 | 2 | 1 | .. | 11 |
| 90–94 | 14 | 15 | .. | .. | 29 |
| 95–99 | 34 | 21 | 1 | 1 | 57 |
| 1900–04 | 65 | 46 | 11 | 2 | 124 |
| 05–09 | 58 | 48 | 2 | 7 | 115 |
| 10–14 | 68 | 80 | 14 | 12 | 174 |
| 15–19 | 50 | 100 | 6 | 24 | 180 |
| 20–24 | 9 | 45 | 1 | 8 | 63 |
| 25– | .. | 1 | .. | 2 | 3 |
| Totals | 306 | 358 | 36 | 56 | 756 |

Senior registrars in the chest service are distributed as follows (whole of Great Britain): first year 24, second year 18, third year 4, fourth year 9, others 10; total 65 (England and Wales 57, Scotland 8).

The inference seems to be that in the next five years some 20 retirement vacancies for consultants may be advertised in England and Wales. For these posts the potential field of applicants drawn from S.H.M.O.s and senior registrars is 415. These figures are very disturbing and they must surely deter any young man recently qualified from entering the chest service.

This obviously has a bearing on the future efficiency of the chest service, which must constantly hope to encourage able young men to join its ranks.

The Strachan committee's report, valuable though its recommendations are, does not go far enough. An urgent and searching investigation of the chest service is required. The aim should be to establish conditions of service which will promote confidence in the future (for without such confidence no-one will wish to enter the service) and also provide broad long-term plans in view of the changing pattern of tuberculosis.

Churchill Hospital,
Headington,
Oxford.

J. M. BLACK
W. S. HAMILTON
GRAHAM W. POOLE.

## WHO ARE THE INFECTORS?

SIR,—In your editorial (Nov. 26) you stress the need to find the unknown infectors and you write off the known patient with chronic tuberculosis and positive sputum in the sentence: "Once diagnosed practically all but the recalcitrant and unteachable soon cease to be a menace to public health."

From a fairly long acquaintance in general practice with the problem of the middle-aged and elderly patient with tuberculosis whose disease is chronic and non-progressive but who still has tubercle bacilli in his sputum, I think that this problem is still underestimated and needs a more active approach.

I have at this moment 2 patients in this category whom I visit fortnightly to impress on them the need for segregation, and who I know pay fairly frequent visits to public-houses.

Another patient with fibroid phthisis and occasional bacilli in his sputum, when convalescent from an injury in a surgical ward, would have been returned to his family, including 2

grandchildren, in a 3-room back-to-back house because he did not require active sanatorium treatment and therefore could not be admitted to a sanatorium. It is not unusual for the children to be hastily ejected from the room of an infectious patient before the front door is opened to the general practitioner.

We can write off these patients as ignorant, unteachable, and recalcitrant, but we cannot write them off as sources of infection.

When a middle-aged man who has had bronchitis for years is told that he now has tuberculosis, that he is infectious, and that he must shun the club and the public-house, he usually accepts this and follows the advice for the first few months; but if chemotherapy does not give him back his liberty he gradually resumes his former habits.

If we want to keep him away from susceptible groups we must do more than admonish him. In Birmingham there is an occupational-therapy centre, but it appears to be patronised by the younger age-groups; distance from home and cost of materials appear to discourage some patients from using it.

There appears to be a definite need for a hostel to house the chronic tuberculous patient who cannot be made non-infectious by chemotherapy and may occupy a bed in a sanatorium or, worse still, in a lodging-house, because there is nowhere else for him to go.

It is difficult to devise methods to keep these patients occupied at home, but suitable day centres and extension of sheltered factories within easy reach might help the ambulant patient.

Once the patient feels that there is no more to be done for him and contact with his medical advisers and ancillary services becomes infrequent he tends to return to his former mode of life and social contacts.

Birmingham. M. BARROW.

SIR,—Dr. Chalke's interesting letter last week prompts me to draw your attention to a promising infector pool, over which a fly or two might be cast.

Many years ago when I was a "locum" in a country practice I had the sputa of all the "chronic bronchitics" examined for tuberculosis and bagged five new cases, including a brace of grandfathers. The elderly person with tuberculosis, which is almost saprophytic in them, is not uncommon; it may be a new infection, as apparently it was in the case of Sir Arthur Keith, which he tells us about in his autobiography, or, far more commonly, it is a return of a purposefully forgotten youthful nightmare. I suggest a trial in one area where the sputa of all chronic bronchitics, asthmatics, all those suffering from chronic cough (especially those who say "I know it's just the fags"), and all who have had three or more bottles of expectorant or cough-sedating mixture should be examined—*and cultured*. This would entail a close coöperation between the G.P.s, the patients, and the public-health authorities; but if the same amount of vim were put into eradicating tuberculosis as the agricultural committees are putting into the extermination of the rabbit it should not be beyond the wit of man.

There is another point about your "incomplete victory" on which I should like elucidation, and it is this: many reports tell us that isoniazid-resistant bacteria make feeble growths which die out. Does the same thing happen in human beings? When a patient is reported as having isoniazid-resistance, it may mean that only 1% or less of his bacteria are so resistant and that his symptoms depend on the 99% that are not. Also when a resistant patient infects someone, and resistant bacteria are found in the infected person, it may mean that these resistant bacteria are but harmless camp-followers of the lads who cause the caseation, cavitation, and concern. Are there any clinical reports on patients who might reasonably be supposed to have only isoniazid-resistant bacteria—people who have been taking isoniazid neat for a year or so? When one considers how easy a thing it is to swallow a few tablets of isoniazid without the slightest discomfort ensuing, this seems to me to be a very important point.

Beckley, Rye. C. G. LEAROYD.

SIR,—Your leading article states an important problem. May I add to your list of solutions?

In South Warwickshire in 1954, 19% of new cases of pulmonary tuberculosis had extensive disease (group III); the majority of these patients were over 40 years old. On average each had more than two abnormal symptoms. A general practitioner tells me that he refers to hospital under 1% of the patients that consult him. I believe that this figure applies to most of the country. Surely then, the first step to reduce the "infector pool" is to radiograph the remaining 99% of general-practitioner patients, thus obtaining a yield of 2% pulmonary-tuberculosis cases. The value of this method was first demonstrated in 1944 by Toussaint and Pritchard.

Most X-ray departments in general hospitals are working to capacity, and only a handful have been able to establish routine radiography of outpatients and inpatients. Development on these lines has almost come to a standstill owing to restricted capital works. Furthermore some patients recommended to attend hospital fail to do so because of social and economic restraints. These facts suggest that radiography should be taken to the patient. This could be achieved by means of small easily transported photofluorographic units exposing roll film and sited for periods of a few weeks either in or very near general practitioners' surgeries. The main problems would be accommodation and staffing, and their solution would involve regional hospital boards, local authorities, and executive councils.

Cases of tuberculosis in part-III accommodation in Warwickshire are common, and I entirely agree with the substance of Dr. Marsh's letter (Nov. 26). He rightly states that there is need for segregation of patients with tuberculosis. The majority of welfare committees are reluctant to recognise that such ambulant cases exist and fail to offer adequate facilities in part-III accommodation. This lamentable state of affairs helps to perpetuate the "infector pool" to which you have rightly drawn attention.

Chest Clinic,
Warneford Hospital,
Leamington Spa. P. G. ARBLASTER.

SIR,—The difficulty in finding a common denominator for the unknown infectors—i.e., apparently fit persons with chronic infectious tuberculosis—has been responsible for a diversity of policies in mass radiography, ranging from attempts at examining whole communities, to more detailed schemes which aim at pinpointing the odd case.

Is it not possible to narrow down the search for the infector to a tangible group of people?

They have in common a tendency either to defer radiographic examination until alarming symptoms force them to seek medical advice, or else to refuse at all times to use facilities for radiography. Experience in mass miniature radiography makes it possible to suggest a number of reasons for this attitude: (1) fear of losing employment and causing hardship to dependants; (2) already existing economic insecurity; (3) superstition and low intelligence; (4) feckleslessness and general lack of interest in anything but the bare essentials of life.

Any one, or any combination, of the above conditions in a group of persons could be instrumental in the formation of a pool of infectors. Given favourable local conditions the perpetuation of the disease in the young would be assured, while they themselves could in turn constitute a new potential pool.

It is not suggested that chronic infectious tuberculosis is confined to any one stratum of the population; it is, however, probable that the delay in diagnosing the disease is greater in those among whom the above conditions are more likely to be found.

These considerations point to a social and economic denominator. Provisional figures for a period of three years in the Islington static unit suggest a connection between the type of disease and social groups as defined in the 1951 Census for England and Wales. They suggest that social groups IV and V should be seriously taken into account when searching for cases of tuberculosis long overdue for diagnosis. This explanation would account for the present lower discovery-rate of pulmonary tuberculosis in large organised groups in which the number of semiskilled and unskilled workers is small, and it would narrow the field to those communities in which groups IV and V form a considerable proportion of the population.

The problem of how to bring these groups to the X-ray screen on a voluntary basis is a different matter.

Mass X-ray Unit 5D,
Islington, London, N.5. G. Z. BRETT.

SIR,—Your leading article stresses the value of the X-ray machine in tuberculosis case-finding, particularly when used on certain occupational groups having close and frequent contact with a large public. There are two methods of attack with the X-ray machine.

First there is the selective technique by which certain specified groups known to have a high morbidity, such as Dr. Marsh's (Nov. 26) lodging-house occupants, contacts of known tuberculous patients, contacts of infected school-children,[1] and patients with symptoms referred by doctors.

Secondly there is the mass technique by which whole communities are examined radiographically at intervals (this is widely practised in Scandinavia and Holland).

In order to use the first method successfully it is necessary to know a great deal more about the epidemiology of tuberculous infection. Such questions as the following are still not answered with certainty:

How close must be the contact and how large the dose of tubercle bacilli? What is the effect of a single small dose compared with repeated or large doses? How is infection related to morbidity at different ages, particularly in the young adult? Does infection occur most frequently at home or at work? Does any occupation carry a high risk of infection or morbidity? What effect has milk-spread bovine or human infection on the epidemiological pattern of infection and disease?

The regular routine use of the tuberculin test can help us to answer these and many other questions.

van Zwanenberg,[2] studying infection and morbidity in child contacts in the home, showed that the patient with directly positive sputum was responsible for nearly all morbidity, whereas the patient with a sputum or laryngeal swab positive only on culture was responsible for a great deal of infection but little or no disease.

A recent tuberculin survey of school-children in a small town in East Suffolk known to have one milk-supply infected with tubercle bacilli showed that by taking a complete history of the child's milk-supply since birth it was possible to determine not only which milk-supply had been infected but also the time at which infected supplies had ceased.

Our experience, like that of others, of detecting naturally infected school-children suggests that a large amount of this infection occurs in the home, particularly in the preschool child.

These three examples indicate what can be done in small surveys in collecting information on the epidemiological behaviour of the tubercle bacillus. Extension of this technique of regular routine tuberculin testing to other groups and ages in different environments will in time give us a better understanding of the methods of spread and the human response to invasion by the tubercle bacillus.

Time is short, and as you say, "as B.C.G., now and in the future, may well interfere with the value of the tuberculin test, we should see to it that both weapons are used intelligently and as far as possible not allowed to blunt themselves by needless clashing."

A more complete understanding of the epidemiology of tuberculosis will enable us to direct our case-finding and preventive methods, including preventive vaccination, more skilfully.

Chest Clinic, St. Helens Hospital, Ipswich. CHARLES J. STEWART.

1. MacDougall, I. A., Mikhail, J. R., Tattersall, W. H. *Med. Offr.* 1951, **86**, 253; *Brit. med. J.* 1953, **i**, 64. Davies, J. V. *Tubercle*, 1955, **36**, 69.
2. van Zwanenberg, D. *Tubercle*, 1955, **36**, 238.

## MUSCLE IMBALANCE IN SCOLIOSIS

SIR,—May I answer some of the points raised by Dr. Basmajian (Nov. 26)?

Firstly it is true that orthopædic surgeons sometimes use the word strength, as applied to muscles, ambiguously, especially when they are discussing deformities due either to upper-motor-neurone lesions or to reflex spasm secondary to irritation of joints. In such circumstances a muscle is often said to be stronger when we really mean that it is the site of abnormally frequent contractions or that its tone is greater than normal. By convention, in anterior poliomyelitis and other lesions of the final common path, the word strength is used to denote the tension produced by a maximal, voluntary, isometric contraction; this is the sense in which the word is used in our paper. It is usually believed that strength in this sense is an expression of the number of muscle-fibre contractions in a given time. We do not claim or wish to suggest that there is a direct mathematical relationship between muscle-strength and the amplitude and frequency of motor-unit action-potentials. Our cumbersome notation of (+)s and (0)s was used in order to avoid giving such an impression, as we know from experience how the Medical Research Council grading of muscle strength in numbers may lead one to assume that grade 4 is twice as strong as grade 2. We do, however, believe that if, for example, the spinal muscles on the left side show either a few, small, infrequent action-potentials, or none at all, while those on the right side show many, large, and frequent potentials then it is reasonable to say that the muscles on the right are acting more strongly or show greater activity.

With regard to fibrillation potentials we did not record these although they were observed occasionally; but in most of our cases the disease was of long standing and one would not expect many fibrillation-potentials from atrophic, fibrous, non-contractile fibres.

We do not claim that electromyography provides a complete picture of muscle activity, but we do suggest that it is one way of examining the activity of muscles which cannot be examined by ordinary clinical methods.

Secondly we did consider the possibility of the muscle-imbalance being secondary to the deformity; in its original draft our paper contained a long discussion of this and other theories. We decided that the inclusion of such material would have made the paper unbalanced; and accordingly some of the theoretical aspects have been incorporated in another paper which, it is hoped, will be published in one of the special journals.

Finally to answer the question whether I advised my colleagues to try the suggested operation, the answer is No—for two reasons. Firstly those patients who came from colleagues were referred for a specific investigation, not for advice on treatment; and secondly I do not think that our hypothesis is sufficiently certain to justify its clinical application. What we said was: "*if* the deformity is due to unequal muscle action, *then* weakening the stronger muscles should prevent the deformity," and we suggested one way of diminishing the action of the deep rotator muscles. An analogous statement about the foot would be: "*if* equinus deformity is due to the balance between the anterior and posterior tibial muscles being upset in favour of the latter, *then* weakening the calf muscles should prevent the deformity; one way of doing this is to divide the tendo achillis."

The practice of medicine and surgery is mainly a traditional craft; and innovations should be adopted

only with caution and if they are based on good scientific evidence. Our article was not meant to be a plea for a speculative operation—which, as far as I know, has never been done. We do suggest that the activity of the deep spinal rotator muscles should be investigated in every patient with paralytic scoliosis. If, in some patients, imbalance of these muscles appears to be an important factor, then consideration might be given to correcting this imbalance.

In a traditional craft suggested innovations nearly always provoke resentment. Fortunately *The Lancet* provides a means by which new ideas can be proposed, criticised, discussed, and confirmed or refuted—dispassionately and scientifically. That is why we submitted our original article and is also my excuse for this long letter.

Robert Jones and Agnes Hunt
Orthopædic Hospital,
Oswestry.

ROBERT ROAF.

## IN THE MENTAL HOSPITAL

SIR,—I am sure that the series of articles under this heading has been read with profound interest by all who are not satisfied with the status quo. As an occupational therapist who has been on the staff or visited some of the hospitals mentioned, I would welcome many of the ideas suggested; and although some seem visionary, it may be that their main defect is that they are well ahead of their time—at least in this country.

There are three points, only briefly mentioned hitherto, which I would like to stress.

1. There is a definite difference (although not always appreciated by institutional staff) in the function of the average ward (bed area) between the mental hospital and the acute general hospital. In a general hospital the ward bed is the "workbench" on which the patient is "serviced" (if that is not being too impersonal) and then passed on for consummative treatment via the outpatient department. In the mental hospital, the ward bed is of no greater therapeutic value than a bed at home. The main treatment centres should be the psychiatrist's consulting-room, occupational-therapy and other work centres, the gymnasium, the social club, the sports field, and (dare one hope?) extramural activities even to the extent of part-time employment in local industry. (Darenth Park Hospital is a good example of this last activity.)

In my first hospital appointment I was asked to organise an occupational and work therapy programme for the acute male cases, and for this purpose I was given one of the smallest, darkest, and dirtiest rooms in the building. Before long both the patients and I were encouraged by having the largest and brightest ward cleared of beds and put at my disposal as a treatment centre.

In the mental hospital the ward should be regarded as a dormitory. Pride of place and finance allocations should be given to the active treatment centres.

2. Dr. Martin has reminded us, in his article last week, of the often insidious dangers of the staff as well as the patients becoming "institutionalised." Thinking especially of the nurses, I cannot help feeling that working a 96-hour fortnight in premises architecturally reminiscent of the Bastille must often have an institutionalising effect.

3. Little has been said in this series of the very strong power of the artisan-staff trade unions to destroy many work-therapy programmes. If you invite a patient who is, say, a skilled carpenter to repair a ward door, the artisan staff may institute strike action. I find this the bitterest pill of all.

I would like to make two specific recommendations:

(*a*) That local industries around the hospital be encouraged, even to the extent of subsidy, to employ on a part-time basis small groups of stabilised inpatients. They should be accompanied by a trained nurse *not* in uniform.

(*b*) That discussion at Ministerial and T.U.C. level be instigated to work out a new, integrated, and open-hearted policy on the rehabilitation of the stabilised inpatient as an accepted feature in normal industry.

Enfield,
Middlesex.

LIONEL A. BAINGER.

## KOROTKOV'S SOUNDS

SIR,—This is a preliminary announcement of discoveries, which it is hoped to publish fully in the near future, concerning the nature and origin of Korotkov's sounds.

This subject has been investigated with the aid of an electronic oscillometer designed for the purpose, which displays the brachial pulse-wave and also a graph of the amplitude of this pulse-wave, related to the pressure of the cuff of a sphygmomanometer applied to the arm.

The elasticity of arteries has been studied by a method involving mathematical analysis of the oscillometric curve. It has been found that the initial slope of this figure, hitherto considered to be a straight line, is in fact curved. Whereas some of these curves can be described by the formula of compound interest, deviation occurs from this rule in others; this, with evidence derived from other sources, suggests that the curve of the initial slope, which can be related to the volume-pressure curves of arteries, belongs to a group of sigmoid and hyperbolic curves, described by the formula:

$$y = \frac{kx^n}{1 + kx^n} + c$$

y and x are arterial volume and distending pressure, respectively, while k, n, and c are constants. The formula does not seem to have been employed in this connection before.

A study of many photographs of the brachial arterial pulse-wave, and of the propagation of pressure waves in elastic tubes, has led to a theory which is advanced here for the first time, namely:

*Theory 1.*—The arterial system of the circulation of the blood is in a state of harmonic motion.

Further study concerning the behaviour of bodies of fluid set into harmonic motion by rhythmical applied force, of the anatomy and physiology of arteries, and of the velocity of conduction of the pulse-wave in arteries has led to the following conclusion:

*Theory 2.*—Arteries resonate to two forces in each pulse-cycle, these forces being related to production of the heart-sounds.

The actual frequency of the resonance in arteries has been found to be considerably higher than the frequency of the pressure-wave arising in the left ventricle of the heart. Study of the action of reflected waves in arteries has led to a third theory, which is likewise original:

*Theory 3.*—Systems of stationary waves develop in arteries with fixed nodes and antinodes at certain points in the arterial system.

Application of the pressure cuff of a sphygmomanometer to the upper arm, which compresses the brachial artery, has been found in certain cases to alter the wave-length and frequency of resonance in the brachial arterial system, with a change in the system of stationary waves, which accounts for the Erlanger-Recklinghausen index, well known in oscillometric studies.

The utilisation of these theories and observations has enabled harmonic analysis of the brachial pulse-wave, as modified by cuff pressure, to be effected. This has revealed the existence of harmonic vibrations in arteries at certain critical points, which are related to the cuff pressures at which the Korotkov sounds occur.

The formula describing arterial elasticity, the three theories of the arterial system, which might be termed "laws," and the well-known principles of hydrodynamics applying to fluids flowing in pipes, including the theory of Reynolds' number, cavitation, and water hammer, have been applied to explain the production and nature of Korotkov's sounds.

Ely, Cambridgeshire. JOHN E. MALCOLM.

## CŒLIAC DISEASE

SIR,—I am grateful to Dr. French for his letter last week in which he corrects a possible source of misunderstanding in my Charles West lecture, which appeared in your issue of Nov. 26.

Dr. French quotes the last sentence of a paragraph concerning the value of fæcal-fat estimations. Lest there be others who have also mistaken my meaning, I should like to make it clear that throughout the paragraph my remarks concerned the percentage estimation of fat in the dried stool, not the estimation of total fat excreted over any given period.

London, W.1. WILFRID SHELDON.

## BREAST CHANGES IN FIBROCYSTIC DISEASE OF THE PANCREAS

SIR,—I read with interest Dr. Jolly's appeal for information (Nov. 26).

Some three years ago I noticed breast enlargement in two cases of fibrocystic disease during the second half of infancy. I wondered whether the breast might share in the fibrocystic change and discussed the matter with Dr. Reginald Lightwood, who doubted this possibility, pointing out that the breast was not a mucus-secreting gland. I have not since seen a case with enlargement of the breast, but I have arranged for microscopic examination of the unenlarged breast disc in two infants who died of fibrocystic disease in the first half of infancy. In each case the microscopic appearance was normal.

Grimsargh, near Preston. GORDON HESLING.

## AUREOMYCIN, IMPROVED NUTRITION, AND GYNÆCOMASTIA

SIR,—The observation by my friend, Dr. Hugh Jolly (Nov. 26), that breast changes occur in children with fibrocystic disease of the pancreas gives me an opportunity to play a card of low denomination which I have held in my hand for eighteen months.

A man, aged 42 years, suffered from cor pulmonale secondary to bronchitis and emphysema. The pulmonary disorder was complicated by recurring acute infections which were controlled by aureomycin therapy. He was discharged from hospital in December, 1953, taking prophylactic aureomycin 0·5 g. twice daily. His nutrition was much improved and he gained 8 lb. in the three weeks after discharge. On March 8, 1954, the infection relapsed and he was readmitted to hospital. It was noticed that he had gynæcomastia, more apparent in the left breast than in the right. No aureomycin was given for eleven days after admission, and urinary endocrine assays were made during this period and later (see table). I did not at this time associate the gynæcomastia with aureomycin therapy, and a week's further course of 2 g. daily was given. During this time the breasts enlarged and the patient complained of considerable discomfort (see figure). His weight increased from 7 st. 2 lb. to 7 st. 8 lb. during this fortnight. When the aureomycin was stopped the breasts ceased to irritate, but the pulmonary infection later relapsed and oxytetracycline therapy was instituted. Within two days the breasts were again irritable. Liver-function tests were normal throughout his stay in hospital.

I concluded from these observations that both the aureomycin and the oxytetracycline were factors in the production of the gynæcomastia. A probable hypothesis of pathogenesis is that the drugs interfered with either the production or the absorption of vitamin B, one of whose properties is the destruction of œstrogen in the body.[1] It was remarkable how quickly the drugs produced irritation in the breasts. Since this experience I have not used these drugs in the prophylaxis of pulmonary infections in children.

It is possible that improved nutrition, particularly enhanced absorption of protein, may be an additional factor in causation when mucoviscidosis is treated by pancreatic granules. In men who were incarcerated in Japanese prison-camps gynæcomastia occurred, occasionally during the phase of confinement (and testicular atrophy) but more often on release and during the early weeks of rapidly improving nutrition.[2–4]

1. Briskind, M. S., Briskind, G. R. *Endocrinology*, 1942, **31**, 109.
2. Klatskin, G., Salter, W. T., Hum, F. D. *Amer. J. med. Sci.* 1947, **213**, 19.
3. Salter, W. T., Klatskin, G., Hum, F. D. *Ibid*, p. 31.
4. Platt, S. S., Schulz, R. Z., Kunstadter, R. H. *Bull. U.S. Army med. Dep.* 1947, **7**, 403.

URINARY ENDOCRINE ASSAYS

| Date | Therapy | 17-Ketosteroids (mg. per 24 hr.) | 17-Ketogenic-steroids (mg. per 24 hr.) | Œstrogen (I.U. per 24 hr.) | Gonado-tropin (mouse units per 24 hr.) | Comments |
|---|---|---|---|---|---|---|
| Dec. 9, 1953 .. | Aureomycin 0·5 g. b.d. | .. | .. | .. | .. | Gynæcomastia observed |
| March 8, 1954 .. | Aureomycin stopped | | | | | |
| March 17 .. | Nil | 3 | 4 | 30 | 30 | |
| March 19.. .. | Aureomycin 0·5 g. q.i.d. | .. | .. | .. | .. | Mammary discomfort |
| March 26.. .. | Aureomycin stopped | | | | | |
| April 3.. .. | Nil | 8 | 4 | 16 | 12 | |
| April 11.. .. | ,, | 5 | 13 | 30 | 7 | Recession of gynæcomastia |
| April 13.. .. | Oxytetracycline 0·25 g. q.i.d. | | | | | |
| April 20.. .. | Oxytetracycline 0·25 g. q.i.d. | 7 | 7 | 30 | 0 | Mammary discomfort returned |
| April 23.. .. | Oxytetracycline stopped | | | | | |
| April 24.. .. | Nil | .. | .. | 70 | 7 | |
| April 28.. .. | ,, | 7 | 13 | .. | .. | |
| May 1.. .. | ,, | 7 | 7 | 20 | 0 | Mammary discomfort disappeared but some enlargement persisted |
| May 8.. .. | ,, | 6 | 13 | 20 | 0 | |
| July 13.. .. | ,, | 7 | 9 | 0 | 14 | |

The normal levels of œstrogen excretion for men are usually said to range from 20 to 100 I.U. per day. Whether the fluctuation or the low levels have any significance, I do not know.

I am grateful to Dr. G. C. Paine, in whose laboratory at the Jessop Hospital for Women, Sheffield, these numerous endocrine assays were made by Mr. L. F. Mitchell, PH.D., and Mr. M. J. Level, B.SC., for permission to publish them. Dr. J. F. Scott, after the manner of good house-physicians, drew my attention to the gynæcomastia.

Derby. DOUGLAS HUBBLE.

## XERORADIOGRAPHY

SIR,—Both you and Dr. Allchin (Dec. 3) appear to be very unfortunate in the radiographs you see. In charge of a busy department, I see many radiographs, and the adequate visualisation of bone and soft-tissue structures seems to me commonplace and essential practice. The suggestion that we pursue interesting special procedures while failing in the efficient performance of "everyday" radiography needs to be refuted.

The significance of the illumination and viewing conditions in relation to the subjective contrast and definition of the image does not appear to be fully appreciated by those outside X-ray departments. Often in clinics and wards one sees a good-quality film showing to poor advantage against an illuminator in which 20% of the bulbs are not functioning, while the remaining 80% are in combat with direct sunlight. Or, worse still, the image is sketchily surveyed with the help of the nearest window. Dr. Allchin's reference to the necessity for correct exposures and processing needs to be extended to include the optimum viewing conditions.

Birmingham, 32. MURIEL O. CHESNEY.

## HYPERTENSIVE RESPONSE TO INJURY

SIR,—In your annotation of Nov. 12 you draw attention to an important clinical feature of many patients with moderate and even severe injuries. Under civilian conditions, and particularly when patients are seen early and transfusion is started promptly, a hypertensive response to trauma is less uncommon than is suggested by the experience of Grant and Reeve.[1]

During the past few years we have been studying clinical patterns of response to injury in association with determinations of blood-volume. A phase of hypertension has occurred in nearly 50% of 80 patients investigated. In some of these the increase in blood-pressure is transient and the pressure falls to normal with anæsthesia. These patients are similar in many respects to those described by Prentice et al.[2] from Korea. They have relatively minor injuries and small blood-loss, and clinical evidence suggests that the high blood-pressure may be determined by painful stimuli or psychogenic influences.

In many of our patients with hypertension, however, blood-loss has been greater than 30%; and in these hypertension has not always responded to anæsthesia, nor has it necessarily indicated a good prognosis. Increasingly we have become convinced that within the first two hours after injury there is little correlation between the blood-pressure and the degree of oligæmia. Transfusion needs can be assessed more adequately from the extent of injury than from the pattern of response, except when this consists in an extreme fall in blood-pressure associated with pallor, cold extremities, and a rapid pulse. Commonly such patients have already lost half their blood-volume.

I agree with your statement that "hypertensive response should be viewed against the background of the severity of the injury and should give rise to a cautious attitude and repeated observation." It is not, however, just a question of watching such patients for a later fall in blood-pressure. Such collapse can often be anticipated and prevented by adequate and early transfusion, which is not contra-indicated by a raised blood-pressure.

There remains the problem of the nature of the hypertensive response itself. I have the impression that it is not necessarily either "compensatory" or clinically desirable. I am not certain that "over-compensation" explains anything at all. There is a considerable body of evidence that the over-all nature of the circulatory response to injury cannot be explained solely in terms of blood-volume changes. The nature of the injury and its treatment are relevant. Further elucidation of the mechanisms involved requires consideration of various neurogenic components affecting circulatory patterns. These can be evaluated only against a background of quantitative knowledge of blood-loss and the adequacy of its replacement.[3]

Birmingham Accident Hospital. RUSCOE CLARKE.

## MODIFIED ELECTROCONVULSION THERAPY

SIR,—We cannot agree with Dr. Kelleher and Dr. Whiteley (Dec. 3) that any undue cyanosis occurs with the 'Ectonus' technique of E.C.T.

One of the desirable features of this technique is that respiration is stimulated and the period of apnœa is shortened. In practice we find that cyanosis is rare and is always much less than in straight E.C.T.

The extended tonus stage produced with ectonus is no longer than the clonic phase with straight E.C.T. The Valsalva phenomenon may possibly occur, but in our experience it has not produced any ill effects.

Regarding the fatality and fracture rates with ectonus, we find a great improvement compared with other methods. We have given over 5000 ectonus treatments (over 1000 cases) in the past eighteen months. There has been 1 death and 1 fracture. The fatality was an exceptional case in that the patient had had a lobectomy twelve days before E.C.T. and at this treatment spontaneous pneumothorax developed on the unaffected side. The fracture was an impacted neck of humerus in a woman aged 69. Radiography showed marked rarifaction of the bones.

Many of our cases have been "poor risks," including 2 with recent coronary thrombosis, but we have felt confident to treat them because we believe that ectonus offers a higher degree of safety than other methods.

We feel that the use of muscle relaxants, with or without anæsthesia, should be reserved for the few cases where these are definitely indicated. Thus the majority of patients are relieved of the undeniable anxiety associated with premedication and injections.

R. J. RUSSELL
L. G. M. PAGE
T. M. MOYLETT
R. L. JILLETT
A. BUCKLEY.

Three Counties Hospital, Arlesey, Beds.

## STAFFING LABORATORIES

SIR,—We wish to express our consternation at the proposed grading and salary-scales for medical laboratory technologists which have just been published in draft form.[4] Far from raising the status of the technologist, we fear that the proposed arrangement will have the opposite effect. Meagre salary increases are proposed, and the career value of the profession is threatened by the ridiculous insistence on relating grading either to the number of technical staff employed or to a very vague definition of what constitutes a division of a laboratory.

This unfair method of grading really takes no account of work done or of responsibility, nor of the fact that the senior technologist does most of the work of training juniors.

If the management side persists in its unrealistic attitude, they will in a few years have very few tech-

1. Grant, R. T., Reeve, E. B. *Spec. Rep. Ser. med. Res. Coun., Lond.* 1951, no. 277.
2. Prentice, T. C., Olney, J. M. jun., Artz, C. P., Howard, J. M. *Surg. Gynec. Obstet.*, 1954, 99, 542.
3. Clarke, R., Flear, C. T. G., Topley, E. *Lancet*, 1955, i, 629.
4. *Gazette of the Institute of Medical Laboratory Technology* November, 1955.

nologists to manage. They may perhaps have plenty of girls to fill the junior posts until they marry; but if laboratories in the National Health Service are to have a solid core of experienced trained technologists, something better must be offered.

L. P. SNOW
B. NUTE
A. R. RYMAN
C. H. N. BENNETT
A. DOVER
D. DUNCAN.

Group Pathology Laboratory,
General Hospital,
Neath, Glam.

## RESPONSIBILITY: INDIVIDUAL OR COLLECTIVE?

SIR,—In the Medicine and the Law section of your issue of Nov. 26, you quote a medical advisory committee as having stated that in their opinion the treatment of a patient entering a hospital (in this particular case a mental hospital) is the "sole responsibility" of the doctor in charge of the case. I do not agree with this opinion, and I consider that the apparent simplicity of this formula (superficially so attractive to us doctors) is dangerous in its implications and obscures important medicolegal issues and other important issues which concern the National Health Service. I submit that when a patient enters a hospital he does so believing that he is entitled, not only to the individual "attention" of a particular practitioner, but also to the benefits which he assumes (and therefore expects) will be available as a consequence of his entering a hospital, viewed as an organic unity; that is to say, he believes he is coming under the care of a corporation comprised of practitioners and their auxiliaries, many of whom are likely to be engaged on tasks in relation to his medical welfare, few (if any) of which in fact can be satisfactorily performed in their entirety by any individual practitioner or auxiliary acting alone.

I submit therefore that the "responsibility" for his care and treatment is vested in the "hospital" viewed as a corporate body. Naturally there are particular instances of individual responsibility discernible within that total corporate responsibility; and some of these individual responsibilities may even devolve in fact on lay members of the corporation, as well as on its medical members. The corporate teamwork and organisation prerequisite and implied in most surgical-theatre procedures is, I submit, a very good example in support of my opinions; and the law no longer holds to its former rigid and unrealistic notions that in fact any surgeon can humanly scrutinise and therefore be held individually responsible for each and all of the technical minutiæ in complicated surgical-theatre procedure.

I am of the opinion, moreover, that a governing body (which might be wholly composed of lay members) to some extent and in particular circumstances enters into this organic relationship with the patient. For instance, if a management committee either fails to produce adequate technical facilities or interferes in some way or other with the development or maintenance of corporate feeling (and therefore corporate care and skills) it might be held responsible if, as a consequence of such negligence or such interference, the safety of a patient is jeopardised or an accident supervenes. An instance of the former would occur if an explosion took place in a surgical theatre as a direct consequence of a managing committee having failed to heed the warning of its doctors concerning faulty electrical installations. An instance of the latter would occur if it could be shown that by intrigue or other means the committee had so fractionated the medical services of a particular hospital as to impair the standard of professional work in that hospital. Such a situation would, in my opinion, merit the scrutiny and possibly the censure of a coroner.

The necessity of viewing a hospital as possessing a corporate and organic quality of responsibility towards its patients can, however, best be exemplified when we consider the "firm" system. This, as we all know, frequently results in a patient being seen by a duty officer of one firm in the evening, whereas the next morning (at, say, 9 A.M.) the patient comes under the care and attention of a practitioner who belongs to another firm and thereafter may cease absolutely to be the concern of the first medical (duty) officer who attended him the night before. I submit that it is only by maintaining this principle of organic responsibility out of the hospital as opposed to the notion of "sole responsibility" of the practitioner that we can possibly safeguard the continuity of treatment and responsibility at law which in such circumstances must be held to apply as a necessity.

Moreover it must be borne in mind that the structure of the National Health Service presupposes that registrars require training. Now whatever we mean by this, we must mean that it implies that instruction is to be given on particular matters; and it may turn out that a particular matter on which the registrar requires instruction concerns how to bring into play the medical and administrative and other organic teamwork involved in the proper care and attention and treatment of a particular patient admitted to hospital. It may be that this in turn becomes one of the objects of a coroner's scrutiny. Moreover how can it be maintained that a patient liable to be attended in turn by a registrar, an S.H.M.O., and a consultant is the "sole" responsibility of the most junior member of such a trio?

In the case described in your report, the patient applied in writing to be admitted to a "hospital," committing her welfare in the first instance to the care of the medical superintendent thereof—not mark you as his "sole" responsibility, and not to a registrar. It was the care of a hospital which she sought.

I submit that if our profession allows the corporate and organic unity of our hospitals to be fractionated there will develop logically nothing other than a situation in which every single doctor will become directly responsible to lay management committees through the agency of lay secretaries. This modern (and Socialist) structure of society is opposed to our former organic structure of society, and inevitably involves discussions of propositions derived from a multiplicity of categories and thereby engenders complex results. Where a mental hospital is concerned, I submit that it is at variance with the existing law.

Finally I submit that it is germane to my main thesis to point out that (as I read his criticisms) the coroner concerned in your report was more disposed to criticise the "hospital" than the medical practitioner. The medical practitioner therefore has only the medical advisory committee involved to blame if these criticisms were deflected on to him. In my opinion the coroner was right in his attitude because it did not and could not lie within the power of an individual doctor to heed all the coroner's criticisms, nor did it lie within his power to put anything right which required putting right. This could only be the function of the organic entity—the hospital. When will lay management committees and those who have been responsible for the present structure of our medical services see what an illogical position they have got themselves into? Assuredly, we are all Esaus.

St. Albans, Herts. HAROLD PALMER.

## THE ANAL SPHINCTERS

SIR,—In your annotation of Oct. 15 you remark that while it was accepted that the subcutaneous external sphincter was the cause of the anal fissure and also formed its base

"the internal sphincter wilted under neglect. But doubt remained in some minds[1]; for why should the muscle, seen in dissection undertaken for fissure and termed external sphincter, appear so pale—too pale, it would seem, for somatic origin?"

The reference in this passage was to an article of mine; and the passage suggests that I was in doubt about the function of the internal sphincter. You may be unaware of two other papers of mine dealing fully and conclusively with the new concept of the internal sphincter.[2] The conclusions of this work were based on dissections at operations under local anæsthesia. The external and internal sphincters were marked by black silk sutures

1. Eisenhammer, S. *S. Afr. med. J.* 1953, **27**, 266.
2. Eisenhammer, S. *Ibid.* 1951, **25**, 486; *Ibid*, 1954, **28**, 264.

before operative exposure; and histological sections gave further proof of the correctness of the new hypothesis. The relation of the internal sphincter to Miles's pectan band was fully discussed and clarified.

In 1951 I introduced this work to Mr. Henry R. Thompson at St. Mark's Hospital. Mr. Thompson adopted my operation of "internal anal sphincterotomy" for the cure of anal fissure, and he has been responsible for popularising this technique. It was his further anatomical observations that led the staff of St. Mark's Hospital to publish a revision of their anatomy.

Johannesburg, South Africa. STEPHEN EISENHAMMER.

## THE RENAL DUCTS OF BELLINI

SIR,—During 1954 you published three letters[1–3] referring to my interpretation of the anatomical morphology of the Bellini ducts. Since then the results of further study have been published elsewhere describing the morphology of the excretory tubes in kidneys of the newborn.[4]

It appears that the Bellini ducts join together in pairs forming a hairpin bend which has an "os" with a slit-like appearance situated not at the end, but at its side, and the hairpin itself ends in a conical cul-de-sac.

This anatomical structure of the Bellini duct suggests first, that the os of the hairpin bend may act as a slit-like valve, avoiding a urinary backflow, thereby explaining the difficulty in filling the Bellini ducts during a retrograde pyelogram and second, the collection of mineral precipitate in the cul-de-sac may be the starting-point of the sterile urinary calculus occasionally found at the tip of the pyramid.[5]

Department of Pathology, Booth Hall Children's Hospital, Manchester. F. DURAN-JORDA.

## RADIOPHOSPHORUS IN THE TREATMENT OF CAPILLARY NÆVI

SIR,—Dr. Roe and his colleagues (Nov. 26) claim excellent results in four out of seventeen cases of nævi treated with radiophosphorus, and they include before-and-after photographs of three of these. Each of these photographs is typical of the so-called strawberry nævi which, as Roe et al. say, disappear spontaneously in the fullness of time.

In these three cases the nævi are entirely superficial, and they are not the same as the deeper red or purple, port-wine-stain marks which persist despite any treatment short of destruction of the skin which bears them.

It is essential to differentiate accurately between the various types of vascular nævi before evaluating the effect of treatment, and to appreciate the natural history of the different types. Otherwise the confusions of the past will be perpetuated.

The strawberry nævus, be it superficial, subcutaneous, or both, will eventually clear up on its own, so does not present a very great ultimate problem; whereas the port-wine mark, excluding those in the midline at the base of the nose or on the occiput, does not fade as the years go by, nor has it been convincingly shown that any form of treatment makes the least difference. As Lister[6] pointed out, a history of growth after birth is of the greatest value in the diagnosis of strawberry nævi.

If indeed β-irradiation with radiophosphorus is found to help in the treatment of "port-wine" nævi, this will be a great advance in therapy; but the premature clearing of totally different lesions should not be accepted as evidence of this.

Plymouth. R. D. SWEET.

1. Jones, C. H., Rewell, R. E. *Lancet*, 1954, ii, 290.
2. Ross, J. A. *Ibid*, p. 758.
3. Thung, P. J. *Ibid*, p. 658.
4. Duran-Jorda, F. *J. Anat.* 1955, **89**, part 4.
5. *Lancet*, 1954, ii, 1009.
6. Lister, W. A. *Ibid*, 1938, i, 1429.

## CARCINOMA OF THE BREAST

SIR,—I am very interested in Mr. Heanley's letter last week. Quite simply stated, my custom for the past 6 years has been to do a local mastectomy (with axillary-gland clearance if required), followed by deep X-ray therapy and injections of testosterone. The ages of patients ranged from 40 to 78 years. Results for about 12 cases have been excellent: no recurrence and no secondaries. I simply record the facts, without discussing their interpretation.

Solihull, Warwickshire. E. S. PAGE.

## RECOVERY WARDS

SIR,—Dr. Hex Venn points out (Oct. 29) that an exhaustive list of the advantages of a recovery ward would need more than a letter. But I feel that an outline of them must be repeated from time to time if this important matter is to get the attention due to it. The nursing shortage will progressively exacerbate the problem. I have been most impressed by the efficacy and economy of maintaining such a ward.

1. In the immediate postoperative period, all patients who need it can have special nursing without delay.

2. The equipment and supplies needed in such care are readily available in one area and need not be duplicated elsewhere.

3. More patients can be operated upon and released the same day, after recovery.

4. Emergency operations can be done at any hour without disturbing patients or routine in other wards.

5. Ward nurses are relieved of the care of patients at the time when nurses are busiest and patients need most attention. They need not be hampered by visitors to these patients or to others on the ward.

6. Anæsthetists and surgeons are readily available for emergencies.

7. This is an ideal job for married registered nurses. These trained nurses represent a big loss to the profession and their integration into other aspects of hospital life is difficult.

8. The preoperative patient is saved psychic trauma in that he is saved the spectacle of returning moaning patients, and the postoperative patient does not have his appetite ruined.

There is an excellent account of the subject in *California Medicine* of May, 1953.

One big question is where to put the recovery ward. If all else fails it can be put where the surgeons' and nurses' dressing-rooms are at present.

Boston, Mass., U.S.A. BARRY O'DONNELL.

## POLISH PATIENTS IN MENTAL HOSPITALS

SIR,—In the mental hospitals of England and Wales nearly 1500 Poles, many of them ex-Servicemen, are under treatment. Attention has been drawn in your columns to their situation; for, although they benefit from professional skill and are well cared for, unlike their British fellow-sufferers they lack the support, the encouragement, and the patient sympathy of relatives and life-long friends. One of your contributors suggested that their plight was one which should rouse the humanitarian interest of the authorities.

This association, which is a completely voluntary association, seeks to stretch out a friendly hand to these sad people who in a double sense "sit in darkness." We have pledged ourselves to send to each of these patients a Christmas parcel with a greeting in their own language, and during the coming year to arrange for a personal visit to as many as possible by someone who both understands their distress and speaks their language.

We appeal to all those who remember Poland's tragic loss of freedom and what the Polish pilots did in the Battle of Britain to preserve our homes. We need (*a*) more people to enrol as "friends" at an annual subscription of

5s. 0d.; (b) some hundreds of contributors to our Christmas Appeal Fund. Will your readers please help?

A. R. N. ROBERTS
Chairman, Association of Friends of Polish Patients in Mental Hospitals in England and Wales.

14, Collingham Gardens, London, S.W.5.

### COLLEGE OF GENERAL PRACTITIONERS

Writing as chairman of the postgraduate-education committee, Dr. ANNIS GILLIE expresses the warm thanks of the college to the firms which contributed to the cost of its symposium on the General-Practitioner Obstetrician, held in London on Nov. 20. They were Allen & Hanburys Ltd., Armour & Co. Ltd., British Schering Ltd., Ciba Laboratories Ltd., Cyanamid Products Ltd., May & Baker Ltd., Parke, Davis & Co. Ltd., and the Wellcome Foundation.

## Public Health

### A Panel for the Personal Services

WHEN the National Health Service Act came into force in 1948 a few local authorities combined their health and welfare services in one department. Now the council of the county borough of Southampton have gone a step further. Not only have they brought their health and welfare departments, so closely associated in aims and work, under the unified control of their medical officer of health, Dr. H. C. Maurice Williams, but they have also appointed a personal services panel which includes all the principal officers of the corporation associated with welfare in its broadest sense.

The medical officer of health, as chairman of this panel, will deal with all special accommodation required for old people, handicapped persons, and problem families. He will set up a review committee, consisting of himself, the housing manager, the children's officer, the chief sanitary inspector, and the superintendent health visitor, to consider all cases in these three categories and decide on the type of accommodation needed. These recommendations will be submitted to the personal services panel who have the authority of the council to allocate suitable accommodation without reference to the council committees. It is hoped in this way to reduce the departmental obstacles that have often hindered rehousing.

There is also a scheme afoot to unite some districts into larger areas so that welfare officers working for, say, the education department or the children's department cover the same area as a group of health visitors. When this scheme is put into operation the work will be centred on a district health centre where the welfare officers of the area will meet weekly to discuss their problems and avoid as far as possible duplicate visits.

### Infectious Diseases in England and Wales

| Disease | Week ended November | | | |
|---|---|---|---|---|
| | 5 | 12 | 19 | 26* |
| Diphtheria | 5 | 16 | 5 | 10 |
| Dysentery | 482 | 535 | 618 | 629 |
| Encephalitis: | | | | |
| Infective | 2 | 2 | 5 | 2 |
| Postinfectious | .. | 4 | 2 | 1 |
| Food-poisoning | 143 | 544 | 405 | 212 |
| Measles, excluding rubella | 2327 | 2355 | 2451 | 2521 |
| Meningococcal infection | 26 | 32 | 22 | 26 |
| Ophthalmia neonatorum | 31 | 26 | 26 | 31 |
| Paratyphoid fever | 11 | 12 | 14 | 11 |
| Pneumonia, primary or influenzal | 368 | 442 | 374 | 411 |
| Poliomyelitis: | | | | |
| Paralytic | 154 | 127 | 111 | 91 |
| Non-paralytic | 105 | 99 | 63 | 68 |
| Puerperal pyrexia | 204 | 252 | 224 | 223 |
| Scarlet fever | 794 | 1011 | 1047 | 1131 |
| Smallpox | .. | .. | .. | .. |
| Tuberculosis: | | | | |
| Respiratory | 621 | 677 | 657 | 644 |
| Meninges and C.N.S. | 8 | 15 | 8 | 18 |
| Other | 93 | 94 | 94 | 75 |
| Typhoid fever | 5 | 5 | 9 | 11 |
| Whooping-cough | 948 | 1072 | 1147 | 1184 |

* Not including late returns.

### An Unidentified Illness

Last week we described a mysterious outbreak of headache, dizziness, nausea, and abdominal pain at the secondary modern school at Tottington, Lancashire. Since then, there has been only one further case.

On Thursday, Dec. 1, a girl of 13 felt dizzy in the afternoon at school. She also had some abdominal pain. She went home about 4.30 P.M. and felt sick. Her parents reported that about 8 P.M., she was in a "faint" for about seven minutes. When she recovered, she had "no use in her legs." At 9.30 P.M., she vomited a considerable quantity of fluid. When seen next morning her temperature was 97·8°F and pulse-rate 80. The pupils were within normal limits. The school doctor thought there was definite slight inequality under uniform lighting conditions. She was still slightly dizzy.

The cause has eluded the most careful inquiries, but it still seems likely that these illnesses were due to fumes of some kind, possibly from the low chimney, which is only 31 feet above ground level and has two large boilers and a small domestic boiler attached to it. On the other hand, the delayed onset of symptoms is hard to explain.

## Parliament

### The Ban on Heroin

IN the House of Lords on Dec. 1, Viscount ELIBANK asked the Government whether Dr. E. A. Gregg, the chairman of the Council of the B.M.A., wrote to the Home Secretary early in November stating that he was convinced that the decision to ban heroin was exceedingly unfortunate; whether the Government were aware that Dr. Gregg had also stated that he and the members of the association who were on the Standing Medical Advisory Committee were not on it as representatives of the association, and that it was most regrettable that the B.M.A. as an association was not consulted as regards the ban so that the opinions of doctors thoroughly representative of the profession might be obtained regarding the use of heroin; and whether in all these circumstances the Government would consider appointing an ad-hoc committee to inquire into the position, and of postponing the operation of the ban pending the committee's report.

Lord MANCROFT, joint parliamentary under-secretary of State for the Home Department, said that as a debate on the subject was to take place in the House on Dec. 13 he would restrict himself to a short statement. The possibility of dispensing with heroin in medicine was considered in 1950 when the Government were advised by the bodies which advised them in medical matters that it would be justifiable to prohibit the use of heroin in the United Kingdom if international agreement were reached to prohibit the manufacture of that drug. In 1954 the Economic and Social Council of the United Nations adopted a resolution urging all governments to prohibit the manufacture, import, and export of heroin, except for small amounts for scientific purposes. In December, 1954, the Minister of Health consulted his advisory bodies and was told that they concurred with the United Kingdom Government's proposal to accept the resolution of the Economic and Social Council. The Home Secretary announced in the House of Commons on Feb. 18 last his decision to grant no further licences after Dec. 31, 1955, for the manufacture of heroin except for small quantities for scientific purposes or the manufacture of nalorphine. It was not until May last that the first indication that the B.M.A. was opposed to this decision reached the Minister of Health.

The matter was fully discussed with a B.M.A. deputation by the Minister of Health, the joint parliamentary under-secretary of State for Scotland, and the Home Secretary, on July 11. As the Government's advisers adhered to the advice which they had originally given, it was decided that the decision not to permit the general manufacture of heroin after the end of this year must stand and the decision was notified to the B.M.A. on Oct. 17 last.

#### AN INTERNATIONAL PROBLEM

The Government, said Lord Mancroft, had given the most anxious and sympathetic consideration to all aspects

of this complex problem, including the position and experience of other countries. It was their view that the proposed ban should be maintained. They would, of course, keep its working under constant review in the light of the experience gained.

Viscount ELIBANK asked if Lord Mancroft was aware that his answer was not the whole story, although it would provide food for debate. In the interval before the debate, would not the Government give the most careful consideration to the interests of the many patients, the mitigation of whose sufferings ought to be one of the cardinal points in this controversy, but which was a point sometimes too readily forgotten by some of those who favoured the ban? Lord MANCROFT said that while it was undesirable to go into detailed debate now, he could assure Lord Elibank that the question of suffering of patients was foremost in the mind of the Government when this matter was considered.

Earl JOWITT hoped that when the debate took place Lord Mancroft would be able to consider the possibility of limiting the ban to the export of heroin. Lord HADEN-GUEST asked if Lord Mancroft could say whether the bulk of the best medical opinion in this country was not in favour of the ban on heroin at the present time; that the question of heroin production, manufacture, and use was a world problem and that heroin had already been banned by 54 nations? And was it not desirable that this country should follow suit in the practice here, thus giving a lead towards the disuse of a drug which was not essential and could be, and frequently was, replaced by other drugs. Lord MANCROFT agreed that this drug had been banned by 54 other countries. Lord Haden-Guest's suggestions commanded a certain respect, but were controverted by others. Lord Mancroft felt that it would be better to leave this controversial subject until the debate on Dec. 13.

Lord KINNAIRD said that from a report in *The Times* of Nov. 23, and in a subsequent letter, it seemed that the B.M.A. was not fully consulted. He wondered if the Government could not ensure that such bodies were always consulted as a matter of course. Lord MANCROFT said that whether the B.M.A. were consulted was again a matter of controversy. That would undoubtedly be one of the aspects which would be discussed in the debate. He would confine himself to saying that the Government adhered firmly to the view that they took all the consultation that they properly should have taken.

Replying in the House of Commons to a number of questions on the proposed ban on the manufacture of heroin, Major GWILYM LLOYD-GEORGE, Home Secretary, repeated in much the same terms the statement of Lord Mancroft in the House of Lords. Replying to a further question, he said that the percentage of heroin addicts in the population of the United Kingdom was ·0001%. Heroin was not imported into the United Kingdom. Exports in the twelve months ending on Sept. 30, 1955, were valued at £261.

## APPROPRIATE ADVISERS

Dr. A. D. D. BROUGHTON asked the Minister of Health whether, in view of the concern that had been expressed by many members of the medical profession about the proposed prohibition of the manufacture of heroin, he would take steps immediately to consult practising doctors as a whole as to the wisdom of banning the drug.—Mr. IAIN MACLEOD replied: Before advising the Home Secretary I consulted, as did my predecessors, the Standing Medical Advisory Committee which includes the most highly-regarded medical opinion in the country. This committee when it considered the problem had among its members 19 doctors who were in active practice. I am sure this is the most suitable body to consult.

Dr. BROUGHTON asked the Minister of Health whether, in view of the opinion expressed by a number of practising doctors to the effect that he had been ill-advised on the therapeutic value of heroin, he would alter the composition of the medical advisory committee by including among its members a pharmacologist. Mr. MACLEOD: The Standing Medical Advisory Committee already includes a distinguished member with both pharmaceutical and clinical experience. Dr. BROUGHTON: Is the Minister aware that his decision to ban the manufacture of heroin has shocked many members of the medical profession and has caused serious concern among the public, and will he not consider altering the constitution of the committee by adding other distinguished pharmacologists to it, so that the committee will have among its members a body of individuals understanding the value of drugs? Mr. MACLEOD: The hon. gentleman is switching his ground. He asked me whether I would include among its members a pharmacologist, and I have said that there is already one of great distinction on the committee, namely, Sir David Campbell, who is president of the General Medical Council, and who has recently reaffirmed his views. Perhaps I may add to that a quotation from the *British Medical Journal* of 1949, which stated on this subject that pharmacological opinion has long held that the social dangers of heroin overshadow its therapeutic importance. Therefore, it may well be that if we increased the membership of the committee in the way suggested we would get an even more definite expression of opinion.

Sir ROBERT BOOTHBY: Is it the opinion of the Minister that the medical advisory committee was set up under the Act for the purpose of giving advice on this kind of subject, namely, the therapeutic value of a specific drug? Mr. MACLEOD: The first section of the Act lays on the Minister the comprehensive duty of providing health services for all the people of this country. This clearly comes within the matters which would normally be referred to the committee.

Mr. SOMERVILLE HASTINGS: Is the Minister aware that while the work of consultants, who are so well represented on the medical advisory committee, is to confirm or make a diagnosis and indicate a line of treatment, the carrying out of that line of treatment, and the relief of symptoms such as pain and cough, is often the responsibility of the general practitioner, and ought he not to have consulted the general practitioners before taking this step? Mr. MACLEOD: General practitioners are well represented on this committee, which includes three members of the council of the British Medical Association. All those matters were carefully taken into account by that committee, which included no less than 19 members with active clinical experience at the time of the recommendation to me. Dr. EDITH SUMMERSKILL: Is it not a fact that the members of this committee, representing as they do pharmacologists, general practitioners, surgeons, and physicians, were unanimous in their recommendations, and that similar committees in 54 other countries have recommended their governments in a similar fashion and that their decision has been accepted? Mr. MACLEOD: Yes, it is true that this distinguished committee was unanimous in the opinion that it gave. It is equally true that in the majority of countries similar advice has been tendered in similar circumstances. All the same, I do not want to pretend anything other than that this decision is a desperately difficult one for a government to take, and I recognise that there are sincere differences of opinion on the matter. Sir JOHN CROWDER: May I ask the Minister if he has read the leading article in *The Times* today (Dec. 5), which says clearly that the medical advisory committee is not the proper and efficient body to give its opinion on whether heroin should be banned or not? Would he reconsider the question and submit it to an altogether different body of practical doctors? Mr. MACLEOD: This subject has been referred by four ministers of health of different parties to the same advisory committee over five years. Until the last few days, it has never been suggested that this body was other than the correct one to which to refer it.

## SUITABLE SUBSTITUTES?

Air Commodore A. V. HARVEY: Will the Minister take into account the serious views of sections of the medical profession and the public which have been shown in the Press and in speeches in the last few days, and will he say why it is that in America, where heroin is prohibited, there are about 100,000 drug addicts against the very small number of 53 in this country? Mr. MACLEOD: The responsibility in this matter rests fairly on the Government, and we would not wish to put it on to any other shoulders. We have most carefully and with great sympathy considered all these matters in taking what I said earlier was a desperately difficult decision. As regards experience in America, I have been in communication with the Surgeon-General of that country and I have heard his opinion today by letter, namely, that there are adequate alternatives to heroin available for use by clinicians. Mr. F. J. BELLENGER: While it is difficult for non-medical Members to follow these arguments and counter-arguments, can the Minister say specifically that in stopping or alleviating pain there is any suitable substitute for this drug? Mr. MACLEOD: All one can say on this matter, which is to some extent in dispute, is that we have taken the best medical

advice we could find, and that this is the general opinion. I would recommend hon. Members who are interested in this matter to read an article on the alternatives to heroin in this week's edition of *The Lancet*. If I may add one more point, which I am not sure everybody realises who thinks that this matter is perhaps of small importance here—which it is in relation to the number of addicts we have—it is that in this country we produce not a small quantity but about 70% of the world's heroin. Dame FLORENCE HORSBRUGH: Might I ask whether in the article in *The Lancet* it is made clear what alternatives are being used and found successful in, say, Canada and the United States? Mr. MACLEOD: Yes, that matter is specifically covered by quotations from American textbooks and, as I have indicated, I, or rather my chief medical officer, has been in touch with the Surgeon-General of the United States on their experience of this matter.

Mr. HERBERT MORRISON: Would not the Minister agree that there is something to be said for considering the production of a white-paper in which the issues could be canvassed, the arguments set out, and the conclusions of the Government stated? Mr. MACLEOD: I am very ready to consider that suggestion. This is not a question of pure black and white in which one can say finally that one opinion is right or another is not. In the last resort, it is a matter for judgment and, therefore, decision by the Government. I am anxious, if I can, to carry public and medical opinion with me on this matter, and I will be glad to consider any steps I can take to make people better informed.

Mr. DAVID PRICE asked the Minister whether, in determining to ban the manufacture of heroin, he was aware that there was no adequate substitute for heroin in the symptomatic treatment of cancer of the lung.—Mr. MACLEOD: In advising the Home Secretary on the proposal that heroin should be banned, I was guided by the advice of my Standing Medical Advisory Committee. After anxious and sympathetic consideration the Government have not felt justified in departing from that advice.

Dr. BROUGHTON asked the Minister what consultation he had with the Medical Research Council on the question of suitable, adequate, and equally effective substitutes for heroin before he reached his decision to ban the manufacture of the drug.—Mr. MACLEOD: I did not consult the Medical Research Council direct but before tendering to me its advice the Standing Committee consulted the British Pharmacopœia Commission who had in turn consulted the M.R.C. before the monograph on heroin was deleted from the *Pharmacopœia*.

## Effects of Noise and Vibration on Health

In the House of Commons on Dec. 2, Sir LIONEL HEALD drew attention to the detrimental effect of noise and vibration on the health, well-being, and efficiency of the nation, and urged the need for more effective measures for the protection of the public. A great deal could be done about noise, and much had been done already. Failure to appreciate the efforts of those who had tried would be unfair to the pioneers in medicine, science, and industry, such as, for example, the late Lord Horder and his followers. Recently, important work had been done at King's College Hospital by Mr. Littler and others. But some people seemed to think that nothing need be done. Lord Horder had said that the cause of most of the trouble with noise was selfishness, and the House of Commons, in moulding public opinion, could do good work. It would be excellent if some single department of the Government or member of the Government could be made responsible for the subject.

Mr. H. A. MARQUAND asked whether the Government were considering introducing some system of periodic medical examination of workpeople in places where excessive noise prevailed. By such means, he thought, the onset of inner-ear deafness could be detected and the worker could be removed to a more suitable occupation before the damage went too far.

Sir HUGH LUCAS-TOOTH, joint under-secretary of state for the Home Department, said that no-one would deny that the background of noise could cause distraction, or even acute irritation, to people who had not been able to adjust themselves to it, but there was no medical evidence that this background of noise had any effect on health or efficiency. The Medical Research Council had considered whether this was a matter which could be made the subject of research, but it had concluded that it was too intangible for any measurable results to be obtained. Such medical research as could be carried out was concerned with particular noisy occupations.

Exhaust noise, he admitted, could not be eliminated completely, but it could be reduced to a reasonable level by efficient silencers. The aircraft industry was also alive to the need for noise reduction, not only in the public interest, but for passenger comfort. Supersonic bangs were an inevitable phenomenon of aircraft flying supersonically, but most supersonic flying was directed out to sea. Over land there was a general minimum height of 30,000 feet. Exceptions to this limit were made only with special authority. For some years the Building Research Station of the Department of Scientific and Industrial Research had been studying the protection of people from noise inside buildings. Means were also being devised to reduce the transmission of sound. The question was largely one of cost. Satisfactory methods of sound insulation had already been developed, and efforts were now being made to reduce the expense.

Noise was one of the perennial problems of hospitals. A report on the subject from the committee of the Central Health Services Council had been circulated by the Minister of Health to all hospital boards and committees. Inquiries were constantly made by the Minister's medical and nursing officers when they visited hospitals and there was evidence that much had been done to improve the position. The effect of noise in factories had been fully investigated by the Medical Research Council through its Industrial Health Research Board. One of the results of that work had been to determine the noise-level above which serious damage was likely to be caused to the hearing. An investigation made in noisy weaving-sheds showed that the wearing of ear-defenders could increase personal efficiency. Investigations at present being carried out were expected to throw light on the more general psychological effects of noise.

## QUESTION TIME

### Capital Punishment

Mr. SYDNEY SILVERMAN asked the Home Secretary if he would bear in mind that even among the dwindling number of persons who desired in some cases to retain the death penalty there was a universal feeling that the law, in its present form at any rate, could not be defended. In those circumstances would the Home Secretary reconsider the matter?—Major LLOYD-GEORGE: It is important that the present state of public opinion should be ascertained in this matter, but surely there is no better place for that than this House.

Replying to a further question, Major LLOYD-GEORGE said that he could not hold out any prospect of legislation on this subject in the near future.

### Discharges from Broadmoor

Replying to a question, Major LLOYD-GEORGE said that the number of patients in Broadmoor Institution at Dec. 31, 1954, was 917. The average number of discharges over the five years 1950–54 was 32.

Mr. W. S. SHEPHERD: Will the Home Secretary say whether, in considering suitability for discharge, he invites opinion from outside sources, or whether he relies entirely upon the Home Office medical services?—Major LLOYD-GEORGE: In most cases we rely on the medical opinion of the staff.

### Alcoholics Anonymous and Prison Visits

Replying to a question asking what approach had been made to him by the Alcoholics Anonymous organisation to allow members to visit inmates of our prisons who had turned to crime through drink, Major LLOYD-GEORGE said that this movement had been allowed to send literature to prison medical officers and had been supplied with a list of names and addresses for this purpose. Members of the movement had been permitted to visit suitable prisoners. Mr. N. N. DODDS: Will the Home Secretary say whether he is hopeful of success from this?—Major LLOYD-GEORGE: While it is too soon to come to a final conclusion about the matter, I can say that the influence of this society has had a beneficial effect on some prisoners.

### Closing of Approved Schools

Replying to a question, Major LLOYD-GEORGE said that action had been taken this year to close 8 approved schools which were surplus to requirements; 5 would close in December and the rest early in 1956. No further closing of

schools was in prospect at present. The reduction in demand for places in approved schools was due largely to the decrease in juvenile delinquency.

### Scottish Patients and Swiss Sanatoria

Replying to a question, Mr. JAMES STUART, Secretary of State for Scotland, said that the Government had decided to end the arrangements for sending Scottish tuberculosis patients to Swiss sanatoria. Patients now in Switzerland would remain as long as their medical treatment required. He could give an assurance that this scheme would not have been dropped had the need for it continued. Only 180 patients were now waiting for admission to sanatoria in Scotland, most of them so as to get into sanatoria near their homes. Of 6049 staffed beds at Sept. 30, 856 were unoccupied, 401 in the western region.

## Obituary

### CHARLES RONALD ST. JOHNSTON

M.D. Birm., F.R.C.P.

Dr. Ronald St. Johnston died in Birmingham last Saturday at the age of 45. Medicine was in his blood; his father and his uncle were doctors, his brother is a general practitioner, and he married a doctor, a fellow resident at the General Hospital and herself a member of a medical family.

When he left King Edward's School he went to the University of Birmingham, where in 1934, in the final examination, he was awarded the Foxwell memorial prize in medicine. He held resident appointments at the General and the Queen's Hospitals and was a medical registrar at the Queen Elizabeth Hospital when it was opened shortly before the war. While holding this appointment in 1945 he was elected to the consultant staff of the United Birmingham Hospitals. This hospital had grown out of an amalgamation of the General and Queen's Hospitals, and St. Johnston liked to claim a family relationship with Dr. Johnson, a physician who had served the Queen's Hospital in the middle of the last century. He was appointed also to the staff of the Manor Hospital, Walsall.

During the war he was in the E.M.S., and later in the R.A.M.C. where he held the rank of lieut.-colonel. Birmingham University awarded him the degree of M.D. in 1946 and he was elected to the fellowship of the Royal College of Physicians in 1951.

C. G. P. writes: "Though particularly interested in diseases of the alimentary tract, Ronald St. Johnston remained a general physician. He wrote little and he was wont to regret that he lacked the mind of the research-worker, but he practised and he taught the art of medicine. His colleagues turned to him with their troubles because they knew his worth, the care with which he weighed up a clinical problem, his gentleness, his sympathy, and his fearless honesty. He was an accomplished mimic and used this ability with effect, so that his teaching was clear and stimulating. Many of his friends will remember him as the star of hospital shows, and especially an occasion in 1937 when he 'took off' Mr. Middleton, the well-known broadcaster.

"His pleasures were in his home; he was a keen fisherman and a good swimmer. He was a gay and entertaining companion for he was a born humorist, and his wit was never unkind; his most delightful tales were often told against himself. He faced great anxieties and a long and distressing illness with courage, which came from a firm belief in the truths of the Christian faith."

He married in 1938 Evelyn Mary, daughter of Dr. H. R. Fisher, of Atherstone. She survives him with their four children.

### MALCOLM HECTORSON VALENTINE CAMERON

M.D., F.R.C.S.(C.), F.A.C.S.

WE have received with regret news from Canada of the death of Dr. Malcolm Cameron, a past president of the Toronto Academy of Medicine. For many years he acted as our Canadian correspondent, and the charm and erudition of his informative despatches won him many friends among our readers.

He was born in Bruce County in 1876 and was educated at Woodstock Collegiate Institute and the University of Toronto. As a student he had already begun to write and he was the editor of *Varsity*. He graduated in 1905 and three years later he joined the staff of St. Michael's Hospital. He completed over twenty years' service with the hospital before he retired in 1930 and was appointed consultant surgeon. For many years he was a lecturer at the University of Toronto and a member of the senate.

Despite his work as a surgeon and as a teacher he continued the editorial career which he had begun as a student, and besides contributing to medical and lay journals he edited the *Bulletin of the Academy of Medicine*.

One of his Canadian colleagues, J. W. S., writes: "The passing of Dr. Malcolm Cameron brings to a close the long and brilliant career of a well-loved surgeon. He was a gentle, kindly man who inspired confidence and gratitude among his patients, and respect and affection from his colleagues. By current standards his formal education was meagre, but he had a thirst for knowledge and a love of learning that never waned, and led him to the top of his chosen profession. He had a passion for teaching, and although ill health forced him to retire from the university staff five years ago, even this autumn he continued to take classes on every possible occasion, should a clinician be absent or late for an appointment. For half a century medical students have been inspired not only by his clinical ability but also by his wisdom and graciousness. As an undergraduate, he added to his income by writing a weekly column in the *Toronto Globe*, and throughout his medical career he continued to write not only on surgery but also on the history of medicine. The many papers and articles that have come from his pen attest to his scholarly mind and mastery of English prose. His influence will continue for many years, not only because of the advice and instruction that he gave to so many younger men, but also because they have known this humane, honest, and upright man."

Dr. Cameron, who was a widower, leaves three sons, one of whom is a doctor.

### WALTER JAMES EDWIN LUPTON

O.B.E., M.A., B.M. Oxfd

Dr. Walter Lupton, who died at Oxford on Nov. 27 at the age of 84, had spent half a life-time in the Indian Civil Service before he returned to England to study, and to practise, medicine.

Born in 1871, at Clapham, Surrey, of yeoman stock, he was educated at the Aldgate ward school in London—where, incidentally, he was a chorister in two city churches—and at the City of London School. He went up to New College, Oxford, on a science scholarship, and for a time he seems to have wavered between science and classics. He finally decided to read the latter, and after taking his degree with first-class honours, in 1893, he obtained a high place in the entrance examination for the Indian Civil Service, and proceeded to India in 1894. There he served in the United Provinces, till, for domestic reasons, he retired in 1920. His service ranged from district and revenue settlement work to appointments in the government secretariat and the board of revenue. His career was described as "brilliant" by Lord Meston, one of the governors under whom he served. For his service in India he was appointed O.B.E.

On his return to England, he "submitted himself," as he was wont to say, "to the rigours of training in medicine" and graduated B.M. in 1924 at the age of 53. From his youthful co-students, he won the appelation of "The Old Bean in a Hurry." After qualifying, he served in the Radcliffe Infirmary, Oxford, as casualty officer, and as house-physician. He settled in North Oxford, where he soon had a large private practice. With this, he combined work at the Radcliffe Infirmary, and for many years he was clinical assistant in the E.N.T. department and second-in-command to Dr. Duigan, as official anæsthetist, and anæsthetist to the dental department and to the Oxford Eye Hospital.

In 1936, when the British Medical Association's annual meeting was held in Oxford he gave useful help in its preparation and organisation. Before the late war, when the committee of civil defence was making its precautionary plans, Dr. Lupton was appointed emergency

medical officer, and when war broke out he became secretary of the local medical war committee of the Oxford division and conducted its activities until 1947. At the same time he was deputy group officer from 1940 until 1945.

In 1943 a coronary thrombosis incapacitated him for many weeks but, on recovery, he carried on though he had to curtail his activities. A busy life left little time for writing, but he contributed letters, notes, and articles to *The Lancet*, the *British Medical Journal*, the *National Dictionary of Political Economy*, and the *Journal of the Royal Asiatic Society*, in which he wrote much on Buddhism—a subject which he had studied in India and Ceylon. His interest in Buddhism began while he was an undergraduate at Oxford, where he taught himself Pali and Sanskrit in order to read the Buddhist scriptures in original. Since his retirement in 1947, he had "amused himself," as he said, by writing a chapter and verse record, against the background of great national and international happenings, of how the local medical profession rose to an emergency. "Luppy," as he was affectionately called, has left behind him an honoured name and a record of high endeavour and achievement. To those of us who knew him there remains the memory of a cultured, wise, and very kindly gentleman.

In 1900 he married Sybil, daughter of Major-General Fendall Currie, who died in 1932. The two daughters of the marriage survive him. R. McC.

### THOMAS JAMES EVANS

M.A. Oxfd

Mr. T. J. Evans, who died on Nov. 23 at the age of 80, came to Guy's in 1914 as lecturer in biology. From 1937 until his retirement in 1945 he served also as dean of the medical school, an office which had never before been held except by a doctor. For sixteen years his post was part-time, but in 1931, when the school first received financial help through the University Grants Committee, he was appointed whole-time lecturer.

Born in a small Cardiganshire village, he was fortunate in coming under the influence of a wise headmaster who early recognised his qualities and ability, and encouraged him to continue his studies first at University College, Aberystwyth, and afterwards at Jesus College, Oxford, where he soon made his mark as a zoologist. Later he carried out original investigations at the Marine Biological Station, Naples. As a schoolboy he was almost entirely Welsh-speaking, so that when he first visited London to take the matriculation examination he had difficulty in making himself understood. All his life he read widely and had many interests outside his chosen subject of zoology. Although he spent most of his adult years in England, and became a master of both spoken and written English, he never lost his attractive and musical Welsh intonation, and maintained a passionate interest in the language, literature, and culture of his native country.

Evans had a great gift for stimulating the interest and arousing the enthusiasm of his students, and under his wise guidance the biology department gradually developed into a large, well-equipped department playing a full part in the activities of Guy's. When the 1939–45 war broke out Evans, as dean, took immediate steps to move the preclinical departments to Tunbridge Wells, where within a few weeks students' hostels were set up and laboratory accommodation improvised. Although past the usual age for retirement he never spared himself, but worked incessantly for the welfare of the medical school and the maintenance of the Guy's tradition despite all difficulties. He will long be remembered for his personal charm, kindly nature, and human qualities, which won the respect and affection of all who knew him, and not least of those with whom he was so closely associated during the critical war years.

G. S.

## Births, Marriages, and Deaths

### DEATHS

JAGGER.—On Nov. 30 at the Royal Hampshire County Hospital, Winchester, Francis Field Cunningham Jagger, M.B., F.F.R., of Priors Acre, Abbotts Road, Winchester, aged 80.

## Diary of the Week

DEC. 11 TO 17

### Sunday, 11th

SIGERIST SOCIETY
3 P.M. (Bedford Hotel, Southampton Row, W.C.1.) Dr. A. D. Morris: James Parkinson—Social and Political Reformer.

### Monday, 12th

UNIVERSITY OF LONDON
5 P.M. (London Hospital Medical College, Turner Street, E.1.) Prof. H. M. Weyrauch (Stanford University, U.S.A.): Non-obstructive Urinary Infections.

MANCHESTER MEDICAL SOCIETY
9 P.M. (Medical School, University of Manchester.) *General Practice.* Dr. C. Metcalfe Brown: Preventive Medicine in General Practice.

### Tuesday, 13th

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, W.C.2
3.45 P.M. Prof. Geoffrey Hadfield: Pituitary-dependent Breast Cancer. (Imperial Cancer Research Fund lecture.)
5 P.M. Professor Weyrauch: Landmarks in Uretero-intestinal Anastomosis. (Moynihan lecture.)

BRITISH POSTGRADUATE MEDICAL FEDERATION
5.30 P.M. (London School of Hygiene and Tropical Medicine, Keppel Street, W.C.1.) Dr. J. N. Hunt: Gastric Digestive Function in Man.

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1
5.30 P.M. *Experimental Medicine and Therapeutics.* Dr. R. C. Muehrcke, Dr. R. A. Joske: Renal Biopsy.
8 P.M. *Psychiatry.* Prof. W. M. Millar, Mr. Arnold Bursill: Psychiatry and Psychology.

INSTITUTE OF NEUROLOGY, National Hospital, Queen Square, W.C.1
5.30 P.M. Dr. R. A. Henson: Central Pain, including Painful Phantom Limbs.

INSTITUTE OF DERMATOLOGY, Lisle Street, W.C.2
5.30 P.M. Dr. P. D. Samman: The Erythemas.

MANCHESTER MEDICAL SOCIETY
8 P.M. *Surgery.* Mr. D. C. Racker: Pelvic Exenteration.

### Wednesday, 14th

ROYAL SOCIETY OF MEDICINE
4.30 P.M. *Physical Medicine.* Dr. J. Shulman: Organisation of Physical-medicine Departments in a Provincial Non-teaching Hospital.

INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. H. Haber: Lichen Planus and Lichenoid Eruptions.

ROYAL SOCIETY OF HEALTH, 90, Buckingham Palace Road, S.W.1
2.30 P.M. Sir Weldon Dalrymple-Champneys: Vaccination Against Poliomyelitis.

BIRMINGHAM MEDICAL INSTITUTE, 134, Great Charles Street, Birmingham, 3
8 P.M. *Psychiatry.* Prof. Alexander Kennedy: Human Reactions to Danger.

NOTTINGHAM MEDICO-CHIRURGICAL SOCIETY, 64, St. James's Street, Nottingham
8.30 P.M. Mr. N. L. Eckhoff: Plastic Surgery in Relation to General Surgery.

MANCHESTER MEDICAL SOCIETY
4.30 P.M. *Pathology.* Dr. Harry Harris: Human Biochemical Genetics.

ROYAL COLLEGE OF SURGEONS OF EDINBURGH, Edinburgh, 8
3.30 P.M. Sir Stewart Duke-Elder: Some Problems in Homoplasty with special reference to Corneal Grafting.

ROYAL FACULTY OF PHYSICIANS AND SURGEONS, 242, St. Vincent Street, Glasgow, C.2
5 P.M. Mr. Roland Barnes: Modern Trends in Bone and Joint Tuberculosis.

### Thursday, 15th

ROYAL COLLEGE OF PHYSICIANS OF LONDON
5 P.M. Sir Geoffrey Marshall: Tudor Edwards—His Contribution to the Study of Diseases of the Chest. (Tudor Edwards lecture.)

ROYAL COLLEGE OF SURGEONS OF ENGLAND
5 P.M. Prof. Roger Warwick: Oculomotor Organisation. (Arris and Gale lecture.)

BRITISH POSTGRADUATE MEDICAL FEDERATION
5.30 P.M. (London School of Hygiene and Tropical Medicine.) Dr. R. E. Davies: Biochemical Aspects of Gastric Secretion.

INSTITUTE OF OBSTETRICS AND GYNÆCOLOGY
3 P.M. (Hammersmith Hospital, Ducane Road, W.12.) Mr. D. W. Currie: Carcinoma of Cervix.

LIVERPOOL MEDICAL INSTITUTION, 114, Mount Pleasant, 3
8 P.M. Dr. R. M. Evans, Mr. J. Howell Hughes: Medical and Surgical Aspects of the Treatment of Peptic Ulcer.

### Friday, 16th

INSTITUTE OF OBSTETRICS AND GYNÆCOLOGY
4.30 P.M. (Chelsea Hospital for Women, S.W.3.) Dr. E. C. Fahmy: Pelvic Tuberculosis.

ROYAL MEDICO-CHIRURGICAL SOCIETY
8.30 P.M. (Royal Faculty of Physicians and Surgeons, 242, St. Vincent Street, Glasgow, C.2.) Prof. Robert Cruickshank: Acute Respiratory Infections.

### Saturday, 17th

INSTITUTE OF ORTHOPÆDICS, 234, Great Portland Street, W.1
10 A.M. Mr. J. N. Wilson: Treatment of Club Foot.

# Notes and News

## ROYAL COLLEGE OF PHYSICIANS OF EDINBURGH

LAST Monday an important extension to the library of the Royal College of Physicians of Edinburgh was opened by the Earl of Wemyss and March. This extension is on the first floor of an Adam house adjoining the college's hall in Queen Street. The smaller front room has been set aside as a fellows' reading-room, and the larger front room as a general reading-room; the back room has been fitted to house periodicals and monographs.

This library was founded a few weeks after the college received its first charter from King Charles II on St. Andrew's day, 1681; and since 1846 it has been contained in the society's present hall. It includes some 200,000 books, periodicals, and pamphlets; there are about 400 current journals, and about 500 books and pamphlets are added each year. The library is maintained solely by the college; but by a recent decision any doctor or other suitable person can read there and, subject to simple formalities, borrow in person or by post.

## RADIATION DANGERS FOR THE TUBERCULOUS

At a meeting of the British Tuberculosis Association in London on Nov. 18, Dr. E. T. W. Starkie discussed the danger of the maximum safe dosage of radiation being exceeded in patients under treatment for tuberculosis. Patients submitted to multiple tomographic examinations, and those treated with artificial pneumothorax or pneumoperitoneum and requiring frequent fluoroscopic examination, might receive dangerous doses. Dr. Starkie described a simple filter, consisting of aluminium and copper, which if inserted in the direct line of the rays reduced the amount of soft rays to within safe limits and yet permitted good radiography and fluoroscopy. Other suggestions for reducing the radiation danger included the use of multiplane tomography and the development of high-voltage radiography.

## DENTAL CHANGES IN KERNICTERUS

AT a meeting of the odontology section of Manchester Medical Society on Oct. 24, Dr. R. M. Forrester opened a discussion on Kernicterus and Related Dental Changes. He said that in every case where kernicterus had originated in hæmolytic disease the enamel of the deciduous teeth was disordered. The most distinct evidence of this disorder was a groove on the canines. This change bore little relation to the green pigmentation that followed severe neonatal jaundice; children with green teeth usually escaped kernicterus. In a group of premature infants with cerebral palsy, similar lesions had been found on the teeth, and this suggested that the disturbance might have originated as "kernicterus or prematurity"—without blood-group incompatibility. Similar lesions, but much milder and more restricted, were found in 20% of infants with birth-weights below 4½ lb. The lesions had not been observed in full-term children with hæmolytic disease in the absence of kernicterus, nor had they been found in other forms of cerebral palsy.

Mr. J. Miller remarked that the hypoplastic grooves in the enamel in cases of kernicterus were apparently associated with a neonatal metabolic disturbance. The green pigmentation which often followed severe hæmolytic disease consisted of a narrow band in the dentine of the deciduous teeth corresponding to the neonatal period.

## A CLINICAL EVENING

As a further contribution to good relations between hospital and general practitioner,[1] the London Hospital has given a series of clinical meetings for doctors who regularly refer their patients to the London. Another of these meetings was held on the evening of Nov. 30—with notable success. Sometimes clinical meetings are less effective than they should be simply because too much is on show and visitors who are unfamiliar with the cases or the conditions they illustrate just have not the time to take everything in. But the London's meeting sensibly confined itself to three subjects—suicide, ulcerative colitis, and pulmonary suppuration. Dr. Henry Wilson's talk on the suicidal risk and the suicidal gesture was full of good advice, and many of his listeners may have wished that they had heard it as students. After the patients had been questioned and examined, Mr. Clive Butler discussed some of the features of ulcerative colitis, particularly the indications for surgery; and Dr. Lloyd Rusby spoke of the difficulties of interpreting the significance of a suppurative pneumonia and the importance of bronchial carcinoma as a cause. There will be another clinical evening at the London next month when Sir Russell Brain and Mr. D. W. C. Northfield will deal with some diseases of the nervous system

1. See *Lancet*, 1954, i, 511.

## University of Cambridge

On Nov. 26 the degree of M.A. was conferred on Dr. D'Almero Kok, university lecturer in the department of medicine, and Dr. J. A. Hislop, assistant director of research in the department of human ecology.

## University of London

Dr. G. B. D. Scott, temporary senior lecturer in morbid anatomy at St. Mary's Hospital Medical School, has been appointed to the university readership in morbidy anatomy at the Royal Free Hospital School of Medicine.

Dr. Scott qualified from St. Mary's Hospital in 1942 and took his M.B. Lond. five years later. He has held appointments as junior lecturer in pathology in the University of Aberdeen and as junior assistant pathologist at Worcester Royal Infirmary. His published work includes papers on diagnosis of reticulosarcoma of the thyroid gland and (jointly) on lipomatous pseudohypertrophy of the pancreas, and effects of cortisone and adrenocorticotrophic hormone on bruise dispersion in skin. In 1952 he proceeded to the M.D. Lond.

## Royal College of Obstetricians and Gynæcologists

At the meeting of the council held on Nov. 26 with Mr. C. D. Read, the president, in the chair, it was announced that the Wellcome Trust had offered a grant of £25,000 to meet the cost of the museum in the new college, and a further £5000 for the cost of two research rooms. The museum will be named the Wellcome Museum of Obstetrics and Gynæcology.

Dr. Naguib Mahfouz of Cairo was invited to give the William Meredith Fletcher Shaw lecture in 1956. Sir Arthur Gemmell and Prof. Margaret Fairlie were coöpted to council. The council authorised the establishment of a regional council in South Africa.

Leverhulme research scholarships were awarded to:
J. Gardiner, M. K. Rinsler, J. Walker.

R. W. Forman was admitted to the membership.

The diploma in obstetrics was awarded to the following:
J. G. Abercrombie, D. H. Alltree, T. D. Anderson, B. P. Appleby, G. W. Ashcroft, Betty A. Astle, J. T. B. Bain, D. T. C. Barber, P. J. C. Barry, Rosemary A. Beasley, J. D. Begg, W. P. Bonnici, N. J. B. Bowie, R. G. Brenchley, Miriam Brennan, R. O. O. E. Bretell, Irene P. Brown, W. M. Browne, Elizabeth J. B. Buchanan, E. A. C. Buckell, J. C. B. E. Carreras, D. R. Chase, Saroj Kumar Chatterji, R. M. Clark, D. H. Clarke, H. J. Clarke, A. Clark-Jones, J. D. C. Cook, Albert Cooke, R. Mc. Corfield, I. D. Craig, J. D. Craven, S. C. Cross, W. E. N. Cummings, Joan M. Curtis, J. A. Dand, B. C. Davies, G. J. Davies, K. D. Davies, Madhuri De Peter Dilnot, P. H. Dootson, A. K. N. Dunton, Elizabeth M. C. Dyke, R. P. Dyson, Harry Eaton, D. P. Elam, Rosalind A. Elliott, Gwenda W. Evans, Jill M. Evans, M. J. Evans, Helen Ezra, J. H. Fairley, W. J. Falconer, W. P. Fitt, J. I. M. Forsyth, R. J. Fothergill, Jennifer M. Fowles, R. C. Francis, D. M. Fraser, Alasdair Fraser-Darling, J. R. Freeman, P. J. Frost, I. C. Fuller, M. G. Gelder, A. A. Gibberd, A. G. Gordon, W. J. H. Graham, J. M. Gray, D. N. Guest, Jharna Sen Gupta, Eric Hainsworth, G. S. Hall, D. J. Handford, J. C. Hartgill, Margaret A. Hartshorne, Margaret M. Heley, P. A. Henderson, C. J. M. Hill, R. H. Hill, J. E. Hodgkin, J. M. D. Hooper, P. A. Hopkins, J. H. Hughes, M. J. Hunter, P. J. Huntingford, Ruth Hutchinson, A. J. C. Hyde, G. P. Jeffrey, Claire D. Johnston, J. A. Johnston, W. A. Johnstone, E. L. Jones, K. R. Kidd, P. N. Knight, Margery R. Lane, A. H. Lasbrey, C. E. Lay, Merton Long, J. S. Lord, C. N. R. Loveys, Kathleen M. Lumb, Isabel M. McCullough, M. A. McDonald, John McGlone, Kathleen McKee, M. B. McKerrow, D. G. G. McLeish, Rona Maclean, Sheila Malhotra, Ann B. Marples, Bernard Martin-Smith, E. J. Masters, Geoffrey Matthews, O. V. Maxim, Helen Menzies, A. M. Middleton, R. J. Morgan, Kirshna Mukerjea, Subodh Chandra Mukerji, R. A. C. Mulligan, Ann G. Mullins, D. D. Munro, Jack Nickson, F. G. A. Noon, Khin Than Nu, M. R. Oates, R. G. Orr, D. H. Paterson, J. B. Pearson, J. D. W. Peck, Elizabeth L. M. Perkins, J. H. Peters, Anne T. A. Phillips, E. M. Pilkington, V. D. Pippett, A. P. Poole, A. M. W. Porter, Leslie Preger, Keki Dinshaw Pr nter, J. G. Pritchard, Patrick Quinn, Anne E. Robinson, D. A. Roche, Anne M. Rodger, R. B. Roe, C. A. Rogerson, A. H. Roscoe, Ruth Roseveare, A. O. Russell, A. J. Salmon, D. E. Sharland, F. E. Shaw, D. C. Shields, P. V. Skinner, J. S. Skipper, R. G. D. Small, I. F. Smith, Margaret B. Smith, R. A. Smith, S. R. Somers, Joan V. Stavert, Mary K. Stedman, Angeline Stephen, J. L. Stevens, R. M. Stewart, Sheila A. S. Thompson, V. R. Tindall, Douglas Troup, Arthur Trueman, Maureen A. Tudor, M. E. Tunstall, J. A. Tutton, C. L. Tutty, Anthony Unsworth, Prudence Valentine, N. F. Walker, G. S. Wallace, G. P. Walsh, T. H. M. Warburton, Derek Wardale, D. S. Watson, Marjorie E. Watts, H. E. Wells, J. A. Whillis, C. J. Whitehead, Dorothy J. Whitney, Eric Wilkes, J. C. Willan, J. T. N. Williams, A. R. Williamson, Mary A. Winser, A. J. Winterton, Elaine Wong, Enid M. Wozencroft, N. L. Wright, L. W. M. Yelland, N. W. H. Young.

### University of Glasgow

Mr. Guido Pontecorvo, F.R.S., has been appointed to the newly founded chair of genetics. He is at present reader in genetics and head of the department of genetics in the university.

### Faculty of Radiologists

At a recent examination for the fellowship the following were successful:

George Ansell, Ellis Barnett, D. C. R. Burrows, Sheila M. Cameron, John Hung Chiu Ho, P. A. W. Lea, H. A. Luke, Yumna E. M. Mansour, Basil Strickland (radiodiagnosis); A. M. Jelliffe, Jean K. Ritchie (radiotherapy).

### British Postgraduate Medical Federation

The central office of the postgraduate federation is moving on Dec. 12 from Gordon Square to a new building at 18, Guilford Street, London, W.C.1 (telephone: HOLborn 2716). This building is on a site purchased for the federation by the University of London. It is the first stage of the proposed postgraduate medical centre which will include the medical section of the university library.

### Society of Apothecaries of London

Dr. Neville Finzi, the master, presided over an informal dinner for members and their guests, held in the great hall on Dec. 1. About 130 persons were present, including Dr. Richard Trail, acting senior warden, and Sir Lionel Whitby, acting junior warden. After dinner Mr. W. G. MacKenzie, curator of the Chelsea Physic Garden, gave a talk, illustrated by lantern-slides, upon the garden and its library and their connection with the society.

### Gloucestershire Royal Hospital

A social gathering was held in the board room of this hospital on Nov. 17 when local general practitioners were invited to meet members of the administrative, professional, and technical staffs who had hitherto been "a voice on the telephone" or "a name on a letter." It is hoped that the meeting will become an annual event.

### The Royal Society

Sir Cyril Hinshelwood, Dr. Lee's professor of chemistry in the University of Oxford, has been elected president of the society. Dr. G. L. Brown, Jodrell professor of physiology at University College in the University of London, was elected biological secretary. Other members of council elected included Sir Alan Drury, Prof. J. H. Gaddum, Prof. J. S. Mitchell, and Sir Rudolph Peters.

### Congress on the Pathology of Infectious Diseases

The first Congrès International de Pathologie Infectieuse will be held at Lyons from May 24 to 26. The main subjects chosen for discussion are virus infections of the nervous system and collagen disorders in infectious diseases. Further particulars may be had from the secretariat of the congress, Institut Pasteur de Lyon, 77, rue Pasteur, Lyon, France.

### British Schools Exploring Society

Applications are invited for the posts of an honorary physician and an honorary surgeon for the 1956 expedition to Iceland, leaving about July 28 and returning mid-September, 1956. The cost to each member will be £200, including personal equipment. Applications should be sent as soon as possible to the secretary, British Schools Exploring Society, 2/W Artillery Mansions, 75, Victoria Street, London, S.W.1.

### London Varicose Clinic

The first anniversary of the opening of this clinic, at York Road, Battersea, S.W.11, was celebrated on Nov. 24, when methods used at the clinic were demonstrated. Dr. Simpson Harvey presided; the Rev. Stanley Southall welcomed visitors on behalf of the Battersea Central Mission, in whose premises the clinic is situated; and Dr. Stanley Rivlin, the superintendent, described the work done. He said that, of 140 patients with ulcerated legs who had attended for treatment, 112 were now healed and the other 28 were following the normal healing course. This had been achieved at a clinic which opened only one whole day a week. Patients attended once a fortnight for approximately six visits and they had been able to live a perfectly normal working and domestic life in between. The steadily growing waiting-list of patients underlined the need for a complete specialist hospital.

### Royal Photographic Society

*Medical Group.*—Dr. Keith Simpson will address this group at 16, Princes Gate, London, S.W.7, on Thursday, Jan. 5, at 7 P.M. He is to speak on Crime in Camera.

### Association of Medical Records Officers

At a meeting of this association to be held at St. Bartholomew's Hospital, London, E.C.1, at 6.40 P.M., on Tuesday, Dec. 13, a Canadian film *Science against Cancer* will be shown and there will be a discussion on cancer registration procedure.

### Scandinavian Hospital in Korea

In South Korea a 500-bed hospital under Scandinavian management is expected to be ready for use in January, 1958. Sweden, Norway, and Denmark are to contribute Kr.47,600,000 worth of material, and 80 Scandinavians will be attached to the hospital.

### Society of Chemical Industry

On Wednesday, Dec. 14, at 6.30 P.M. in the rooms of the Linnean Society, Burlington House, Piccadilly, London, W.1, this society will hold the second meeting in their series on Nutrition Requirements and Food Fortification, when Dr. H. M. Sinclair, Miss A. M. Copping, and Mr. J. B. Coppock, PH.D., will speak on vitamins of the B group.

---

In a recent leading article (Nov. 12, p. 1020) we mentioned the difficulty in obtaining supplies of pure 5-hydroxy-indole acetic acid (5-H.I.A.A.) to serve as a standard in the assay of this substance. Messrs. May & Baker (Dagenham, Essex) inform us that pure 5-H.I.A.A. may be had from their new-products division.

Sir Harold Whittingham, director of medical services of British Overseas Airways Corporation, has been re-elected chairman of the medical committee of the International Air Transport Association.

Dr. L. Rendell-Baker has been appointed Fulbright exchange assistant professor in clinical anesthesia at the Mercy Hospital, Pittsburgh, Pennsylvania, U.S.A.

---

CORRIGENDA: *Standing Medical Advisory Committee of the Central Health Services Council.*—A footnote to last week's annotation on Heroin purported to give the names of all who were members of this committee at the end of December, 1954; but it unfortunately omitted those "appointed by the Minister after consultation with representative organisations"—namely, Sir WILLIAM GILLIATT, F.R.C.O.G.; Dr. HORACE JOULES; Dr. H. M. C. MACAULAY; Dr. RALSTON PATERSON; Dr. G. W. H. TOWNSEND; and Dr. S. WAND.

*A Film for Expectant Mothers.*—The film *My First Baby* described in our issue of Nov. 26 (p. 1146) was sponsored by Miss Jean Burton-Brown, F.R.C.S. The National Birthday Trust Fund provided facilities at their house for the preview.

## Appointments

BROWN, MARGARET W., M.B. Edin., F.F.A. R.C.S., D.A.: consultant anæsthetist, Sunderland area H.M.C.

FLYNN, F. V., M.D. Lond.: whole-time biochemist, dept. of clinical pathology, University College Hospital, London.

RAYNER, M. J., M.B. Birm., D.P.H.: senior asst. M.O.H. and school M.O., Dudley.

SAUNDERS, E. G., M.B. Lond.: appointed factory doctor, Whaley Bridge, Cheshire.

STRACH, E. H., M.D. Prague, M.CH.ORTH. Lpool, F.R.C.S.: part-time consultant orthopædic surgeon, St. Helens area.

**Leeds Regional Hospital Board:**

CARTER, J. R., M.B. Lond., M.R.C.P.: whole-time asst. chest physician and deputy medical superintendent, Castle Hill Sanatorium.

HUNTLEY, D. G., M.B. Leeds, D.A.; whole-time asst. anæsthetist (S.H.M.O.), Wakefield A and B groups.

MACLEOD, PEARL A. I., M.B. Glasg., F.R.F.P.S., F.R.A.C.S., whole-time asst. orthopædic surgeon, Harrogate.

**Manchester Regional Hospital Board:**

KASASIAN, A. H., F.F.A. R.C.S., D.A.: consultant anæsthetist, Wigan and Leigh Hospital Centre.

KIRKMAN, N. F., M.D. Manc., F.R.C.S.: consultant surgeon, Withington Hospital, Manchester.

LEVENE, M., M.R.C.S., D. PATH.: whole-time asst. pathologist, South Manchester group laboratory.

MITRA, A. K., M.B. Calcutta, D.O.: asst. ophthalmologist, Stockport and Buxton hospital centre.

WALTON, D. A. H., M.B. Calcutta, D.M.R.D.: whole-time consultant radiologist, Oldham and district hospitals.

WEBER, J. C. P., M.D. Lond.: whole-time asst. chest physician, Barrow and Furness hospital centre.

**South Western Regional Hospital Board:**

MANDLEBROTE, B., M.B. Cape Town, D.P.M.: medical superintendent, Horton Road and Coney Hill Hospitals, Gloucester.

SINGHA, H. S., M.B. Camb., F.R.C.S.: surgical registrar, South Devon and East Cornwall Hospital, Plymouth.

VARMA, R. M., M.B. Madras: registrar, dept. of neurological surgery, Frenchay Hospital, Bristol.

# CHILDREN IN HOSPITAL

## SOME OBSERVATIONS ON THEIR REACTIONS WITH SPECIAL REFERENCE TO DAILY VISITING

R. S. ILLINGWORTH
M.D. Leeds, F.R.C.P., D.P.H., D.C.H.
PROFESSOR OF CHILD HEALTH

K. S. HOLT
M.D. Rochester, M.B. Manc., M.R.C.P., D.C.H.
LECTURER IN CHILD HEALTH

DEPARTMENT OF CHILD HEALTH, UNIVERSITY OF SHEFFIELD

IN recent years there have been many papers about the effect of hospital care on the child. Among valuable reviews on the subject those by Edelston (1943), Bowlby (1951), Prugh et al. (1953), and Capes (1955) are particularly notable. Although these workers and others make it clear that institutional care, with separation from the mother, may cause considerable psychological trauma, they leave many questions unanswered. For instance, how much is the emotional trauma related to the child's age, family, and social background, the frequency of visits by the parents, and the duration of stay in hospital? In particular, does it do any lasting harm to a child to be emotionally disturbed for a few days as a result of admission to hospital? Unfortunately, it is extremely hard to answer these questions. The many papers which we have been able to find refer in general terms to the psychological trauma of stay in hospital, but they do not attempt to define the incidence and extent of the problem, particularly in relation to age.

Any study of psychological reactions in a large group of children is beset with difficulties and fallacies, and it was with full knowledge of these difficulties that we embarked on investigations to determine some facts about the responses of children in hospital, with particular reference to their reaction after visits. There are no "controls" who were not visited. In our view a controlled investigation, which would allow daily visiting for some children but not for others, would be unethical, so convinced are we of the importance of daily contact of parents with their sick children.

### The First Study

Daily visiting was introduced at the Children's Hospital, Sheffield, in April, 1952. At first only 1 parent was allowed to visit at a time, but in January, 1955, both parents were allowed into the ward together. The visiting time is 6.00 P.M. on weekdays and 2.30 P.M. on Sundays.

When daily visiting was introduced, the senior resident, Dr. F. Lees, kept a daily record of the number of visits made, and endeavoured to observe the reactions of the children. It was later decided that other members of the department of child health should keep a more comprehensive record of the effect of visiting, and we prepared a proforma which was to be filled in for every child.

After over a year's work it became obvious that the investigation was unsatisfactory. In the first place observations had not been kept on a small number of children, and this upset the whole study because it might mean that children observed were "selected." They might, for instance, have been included because they reacted in a particular way to visits. Secondly, the proforma allowed replies which were too vague and which would make analysis impossible. For instance, the doctor was asked to fill in, each day, columns headed "behaviour during visit," "behaviour after visit," "behaviour during day."

We therefore prepared a second proforma, details of which are described below, and began again from the beginning. We shall call the first investigation, which included 100 children, series A, but in the analysis of results we shall only refer to the second investigation, which included 181 children (series B), unless the contrary is specifically stated.

### The Present Study

The *proforma* demanded the following information about each child:

Age, name, address, sex, diagnosis, date of admission, date of discharge, hospital ward (one of two), maximum number of visits possible, total number of visits made, cost of travel and time taken in travel for each visit, and reasons given for failure to visit. Previous admissions to hospital were recorded.

On each of the first fourteen days of the child's stay in hospital (if he stayed as long as fourteen days), the following information was required: person visiting (mother, father, grandparent, uncle, or aunt, other person); the child's behaviour during the day, under the following headings: (1) apparently happy, (2) miserable, (3) crying a lot; and the behaviour (*a*) five minutes, and (*b*) thirty minutes after visitors had left, in each case under the headings (I) apparently happy, (II) asleep, (III) crying, (IV) merely miserable. The appropriate mark was made in each of the columns every day.

The day-to-day records were made by the house-physicians, but if they happened to be called away at the time when the observations were to be made, or were away on holiday the observations were recorded by the sister, charge nurse, or resident medical student by arrangement. It was clear to us before the investigation began that the records would sometimes have to be made by people other than the house-physician, because he would inevitably be called away to deal with emergencies, and he would be very likely to be engaged in talking to parents after they had left their children's bedside. It was felt, however, that the simplicity of the observations called for would avoid much in the way of mistakes, though some differences of opinion about the child's behaviour would be inevitable. However desirable, it was clearly impossible that one person should make the observations throughout. The description of the child's behaviour during the day was made by the house-physician after consultation with the ward sister.

#### POSSIBLE FALLACIES

When a child was ill, and was thought to look miserable, it was a matter of opinion whether his behaviour was due to his illness, to his separation from his parents, or both. If a child was unduly silent, it had to be decided whether his silence was due to separation from his mother, or merely to shyness. It had to be left to the common sense of the observer. If a child was in coma, or slept through visiting time, or was under the influence of an anæsthetic, his behaviour could not be usefully recorded and the appropriate note was made so that on that day his behaviour would be excluded from the final analysis. We did not expect that the figures given by the parents for the time taken for travel and for the cost of travel would be absolutely accurate, but we felt that they would give a good idea of the time and cost involved.

Another difficulty arose from the fact that wherever possible when admitting young children we admit their mothers with them, especially if it seems obvious that separation would be difficult for either mother or child. Such cases had, of course, to be excluded from the study, with the result that many children who would have been particularly likely to show emotional disturbances during the day and after visiting were not included in the investigation. Such were the main fallacies of the study.

#### THE CHILDREN

The whole investigation was under the constant supervision of one of us (K. S. H.), and was discussed as

TABLE I—AGE AND SEX DISTRIBUTION OF CHILDREN

| Age (yr.) | Total no. of children | Male | Female |
|---|---|---|---|
| 1 | 28 | 21 | 7 |
| 2 | 17 | 5 | 12 |
| 3 | 20 | 14 | 6 |
| 4 | 12 | 7 | 5 |
| 5 | 26 | 9 | 17 |
| 6 | 18 | 11 | 7 |
| 7 | 9 | 5 | 4 |
| 8 | 9 | 4 | 5 |
| 9 | 15 | 10 | 5 |
| 10 | 9 | 6 | 3 |
| 11 | 8 | 2 | 6 |
| 12 | 5 | 4 | 1 |
| 13 | 4 | 1 | 3 |
| 14 | 1 | .. | 1 |
| Total .. | 181 | 99 | 82 |

For analysis the children were put into five groups ages 1–2 (45 children), 3–4 (32), 5–6 (44), 7–9 (33), and 10–14 (27).

a whole at frequent intervals by the full departmental staff.

All children, aged one year or more, who were admitted to the professorial unit of the Children's Hospital, were included in the study. The only exceptions were children admitted with their mothers, and all patients admitted during three short periods when the wards were being redecorated.

The total number of children studied was 181. The distribution by age and sex is shown in table I.

The average duration of stay in hospital is shown in table II. It will be seen that the younger the child, the shorter his stay in hospital tended to be. 50·6% of the children of 1–4 years of age stayed in hospital seven days or less, as compared with 18·5% of those aged 10–14. A high proportion of the older children who had a long stay in hospital were suffering from rheumatic fever or tuberculous meningitis. 41 of the children had been in hospital before.

## Causes and Frequency of Visiting

The *frequency* with which visits were made by parents is shown in table III. In compiling this and other tables a visit by more than 1 person on a visiting day was regarded as 1 visit.

TABLE II—DURATION OF STAY IN HOSPITAL

| Age (yr.) | Proportion of children in hospital for | | | |
|---|---|---|---|---|
| | 7 days or less | 8–14 days | 15–31 days | 32 days or more |
| 1–2 | 48·9% | 17·8% | 24·5% | 8·9% |
| 3–4 | 53·1% | 15·6% | 3·1% | 28·1% |
| 5–6 | 34·1% | 20·4% | 22·7% | 22·7% |
| 7–9 | 30·3% | 27·3% | 38·5% | 3·1% |
| 10–14 | 18·5% | 37·0% | 14·8% | 29·6% |

It is a striking fact that parents or others made 90·6% of 1587 possible visits during the observation period. The proportion was still higher in the younger age-groups.

In the case of the 3–4-year-olds and 7–9-year-olds, the corresponding figures were 94·0% and 94·1% respectively. 76·7% of the children were visited on every possible day. Only 1 child was not visited at all: he was a defective child of a problem family. In the case of children who stayed in hospital eight days or more, 88·8% of possible visits were made during the observation period. There was no relationship between the frequency of the visits and the sex of the child.

Table IV shows the *cost of visiting* in time and money, and table V shows the relationship between this and the frequency of visits.

The average cost of the round journey was 2*s.* 1*d.*, and the average travelling time for the round journey was 105 minutes. It will be seen that in more than 1 in every 5 children each visit cost 3*s.* or more. For 8·4% of the 181 children each visit cost 5*s.* or more. The round journey in the case of 85% of the children occupied an hour or more in travelling time, and that excludes the time spent in the hospital. In 42·7% of cases visits took two hours or more: in 16% three hours or more: and in 8·8% four hours or more.

It is striking, however, that even when visiting was expensive, a high proportion of possible visits was made. For instance, 74·1% of all possible visits (86 out of 116) were made to children when the visits cost 5*s.* or more per day. 78·4% of possible visits were made when the visits occupied three hours or more in travelling time, and 76·5% (114 out of 149 possible visits) were made when they occupied four hours or more.

As one of the sisters put it, "most parents will move heaven and earth to visit their children in hospital." It should be noted that part of this investigation was being conducted during winter months, and on quite a number of occasions travelling conditions were made very difficult by snow, ice, and fog.

Table VI shows that the mother visited in 73% of cases, either alone or with another person, and the father in 34·1% of cases.

We attempted to analyse the reasons offered by parents for not visiting, but the result was not satisfactory. In some cases

TABLE III—FREQUENCY OF VISITING IN RELATION TO AGE AND STAY IN HOSPITAL (OBSERVATION PERIOD FIRST 14 DAYS)

| Age (yr.) | No. of children | Total no. of visits possible | Possible visits made | Children who had full number of visits | Stay in hospital | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | One week or less | | 8 days or more | |
| | | | | | Total visits possible | Visits made | Total visits possible | Visits made |
| 1–2 | 45 | 329 | 84·8% | 75·5% | 113 | 92·0% | 216 | 80·2% |
| 3–4 | 32 | 255 | 94·1% | 87·5% | 92 | 96·5% | 163 | 92·6% |
| 5–6 | 44 | 414 | 92·9% | 72·7% | 82 | 90·2% | 332 | 93·6% |
| 7–9 | 33 | 318 | 94·0% | 87·9% | 63 | 98·4% | 255 | 96·8% |
| 10–14 | 27 | 271 | 79·9% | 59·2% | 30 | 86·6% | 241 | 78·4% |
| Total | 181 | 1587 | 90·6% | 76·7% | 380 | 93·4% | 1207 | 88·8% |

the house-physician forgot to ask the parents about this at subsequent visits, and the reasons given were varied and often multiple, so that analysis was impossible. In 14 cases visits were missed on account of cost and distance; in 9 cases the presence of small children at home made visiting impossible. Other reasons included illness at home, the non-existence of parents, and a variety of social factors. In 2 cases parents did not visit because they feared that visits would upset their child.

## Behaviour of the Children

Table VII shows the number of children who appeared, during the whole of their observation period, to be emotionally normal during the day and to be undisturbed after departure of their visitors. Taking both sexes together, 32·4% of the children aged 1–4 were apparently normal during the day, as compared with 56·8% of those aged 5–6 and 72·4% of those aged 7–14.

In the younger age-group (1–4) boys appeared to be more liable to be disturbed than girls, for only 25·5% of the boys

TABLE IV—COST OF VISITING IN MONEY AND TIME

| Cost of round journey (average 2*s.* 1*d.*) | | Duration of round journey (average 1 hr. 45 min.) | |
|---|---|---|---|
| Range | | Range | |
| Cost | Percentage | Time | Percentage |
| 0 –11*d.* | 19·1 | Less than 1 hr. | 15·0 |
| 1*s.*–1*s.* 11*d.* | 37·1 | 1–2 hr. | 41·7 |
| 2*s.*–2*s.* 11*d.* | 23·1 | 2–3 hr. | 26·7 |
| 3*s.*–3*s.* 11*d.* | 6·2 | 3–4 hr. | 7·2 |
| 4*s.*–4*s.* 11*d.* | 6·7 | 4 hr. or more | 8·8 |
| 5*s.* or more | 8·4 | .. | .. |

appeared normal during the day, as compared with 43·3% of the girls. This difference, however, is not statistically significant. The situation is reversed in the 7–14-year-olds, 77·4% of the boys being normal during the day, as compared with 66·6% of the girls.

Similar age and sex differences apply to the behaviour of the children after visiting. 13·9% of children of both sexes aged 1–4 were apparently undisturbed after departure of their visitors, as compared with 62·1% of those aged 7–14; 10·7% of the boys aged 1–4 and 19·9% of the girls of that age were apparently unaffected. The corresponding figures for the age of 7–14 were 67·7% (boys) and 55·5% (girls).

It is interesting to note that in series A, the pilot survey, in which all the observers were different from those in the present series, 13·3% of the children aged 1–4 were apparently undisturbed after departure of their visitors, as compared with 13·9% of the present series—a strikingly similar figure. It is clear that the younger the child, the greater is the likelihood of emotional disturbance both during the day and after visiting time.

TABLE V—VISITS IN RELATION TO COST OF VISIT IN TIME AND MONEY (OBSERVATION PERIOD FIRST 14 DAYS)

| Cost of visit | Possible visits made | Time | |
|---|---|---|---|
| | | Duration of travelling | Possible visits made |
| 0 –11*d.* | 93·3% | Less than 1 hr. | 97·2% |
| 1*s.*–1*s.* 11*d.* | 92·7% | 1–2 hr. | 94·7% |
| 2*s.*–2*s.* 11*d.* | 92·9% | 2–3 hr. | 85·7% |
| 3*s.*–3*s.* 11*d.* | 74·7% | 3–4 hr. | 78·4% |
| 4*s.*–4*s.* 11*d.* | 78·8% | 4 hr. or more | 76·5% |
| 5*s.* or more | 74·1% | .. | .. |

The emotional responses of those children who appeared to be disturbed during the day and after departure of the visitors were many and varied: in some cases they only occurred on one or two days, and in others on many of the days at risk. These are some of the comments from the proformas.

(1) Aged 18 months. "Cried all day for his mummy; only stopped when exhausted or asleep. Only one visit. Threw arms round mother and sobbed. After visit, cried for fifteen minutes." (This child was an inpatient for two days only.)

(2) Aged 2 years. "Screamed 'don't come near me' as anyone approached the cot. Refused to eat. Burst into tears every time on seeing his mother, clinging to her. Screamed bitterly on her departure. So fretful and crying so much during the day with outbursts of crying when parents visit that it was thought best to admit the mother."

TABLE VI—THE IDENTITY OF THE VISITOR

| Visitor | Percentage of visits |
|---|---|
| Mother alone | 55·2 |
| Mother and father | 14·1 |
| Mother and grandparent | 1·9 |
| Mother and aunt and uncle | 1·7 |
| Mother and friend | 0·1 |
| Father alone | 19·8 |
| Father and grandparent | 0·1 |
| Father and aunt and uncle | 0·2 |
| Grandparents alone (one or other) | 3·3 |
| Uncle or aunt | 1·7 |
| Other person | 1·7 |

(3) Aged 2 years. "Although the child never cried, I am of the impression that she was very deeply affected by this experience. After visits, quiet and bewildered."

(4) Aged 2 years. "After visit watched the door quietly for ten minutes."

(5) Aged 2½ years. "Took a week to settle in, crying more than most, then was good for several weeks, then became naughty, dirtying the bed, baiting other children."

(6) Aged 21 months. "Happy unless approached, then cries. Irritable, sullen, tearful by day: clinging in visits."

TABLE VII—PROPORTION OF CHILDREN APPARENTLY NORMAL THROUGHOUT THEIR STAY (OBSERVATION PERIOD FIRST 14 DAYS)

| Age (yr.) | Total no. of children at risk* | Apparently normal every day | | | Apparently normal after every visit | | |
|---|---|---|---|---|---|---|---|
| | | Girls | Boys | Both sexes | Girls | Boys | Both sexes |
| 1–4 | 77 | 43·3% | 25·5% | 32·4% | 19·9% | 10·7% | 13·9% |
| 5–6 | 44 | 58·3% | 54·9% | 56·8% | 33·3% | 25·0% | 29·5% |
| 7–14 | 58 | 66·6% | 77·4% | 72·4% | 55·5% | 67·7% | 62·1% |

*Records of 2 children were not used for analysis of behaviour.

(7) Aged 16 months. "Squealing incessantly unless sedated or asleep."

(8) Aged 20 months. "Bright and charming during visits, sullen and reproachful afterwards, wanting to be left alone."

(9) Aged 2 years. "Settled almost immediately. Sat up and received the situation happily. Minimally disturbed. Was outgoing and apparently happy."

(10) Aged 18 months. "Very tearful, bewildered, negativistic. Settled very slowly; never really at ease. In visits, clinging and reproachful. I think that this child was profoundly affected by this hospitalisation, bewildered and insecure."

(11) Aged 3 years. "Lay curled up most of day: would not talk to us. Hugged rabbit. Took a good ten days to settle: till then whimpered if approached, took comfort in his rabbit and thumb. During visits, clinging and asking to be taken home. After visits, cried, cuddled rabbit, and sucked thumb."

TABLE VIII—BEHAVIOUR DURING THE DAY

| Age (yr.) | No. of children at risk* | Disturbed on one or more days | Days on which disturbed | Total no. of disturbance days | Proportion of total disturbance days manifested by | |
|---|---|---|---|---|---|---|
| | | | | | "Misery" | "Crying" |
| 1–2 | 45 | 68·9% | 54·9% | 128 | 75·2% | 24·8% |
| 3–4 | 32 | 68·7% | 44·7% | 67 | 79·4% | 20·6% |
| 5–6 | 44 | 43·2% | 23·8% | 51 | 94·2% | 5·8% |
| 7–9 | 33 | 33·3% | 26·3% | 25 | 96·0% | 4·0% |
| 10–14 | 25 | 20·0% | 17·5% | 11 | 100% | .. |

* Records of behaviour in 2 children not used.

*Example.*—In 10–14 age-group, 5 out of 25 children (20%) were upset for a total number of eleven days (17·5% of the total days these children were observed); all 5 (100%) reacted by "misery" rather than by "crying."

Analysis of the replies to the specific questions on the proforma was more difficult. Table VIII analyses the incidence of behaviour disturbances during the day. The third column shows the proportion of children who were disturbed on one or more days during the observation period. This corresponds to table VII: 68·9% of the children aged 1–2, 43·2% of those aged 5–6, and 20% of those aged 10–14, fell into this category. Table VIII also gives information about the extent of such disturbances. It will be seen that the children in the 1–2 group

TABLE IX—BEHAVIOUR AFTER VISITS

| Age (yr.) | No. of children at risk | Disturbed after one or more visits | Proportion of visits after which they were disturbed | Total no. of days on which disturbance followed visits | Proportion of visits after which disturbance was manifested by | |
|---|---|---|---|---|---|---|
| | | | | | "Misery" | "Crying" |
| 1–2 | 45 | 86·3% | 76·9% | 186 | 27·4% | 72·6% |
| 3–4 | 32 | 74·1% | 61·3% | 109 | 35·8% | 64·2% |
| 5–6 | 44 | 70·5% | 31·2% | 92 | 47·8% | 52·2% |
| 7–9 | 33 | 39·3% | 24·8% | 32 | 87·5% | 12·5% |
| 10–14 | 25 | 32·0% | 20·7% | 17 | 94·1% | 5·9% |

For explanation see footnote under table VIII.

who showed any disturbances at all were disturbed on more than half the days at risk—54·9%. The corresponding figures were 44·7% for the 3–4-year-olds and 17·5% for the 10–14-year-olds. The last two columns analyse the responses shown in the two broad groups of "merely miserable" and "crying." None of the affected older children cried during the day: three-quarters of the affected 1–2-year-olds appeared to be "miserable" during the day, the other quarter "crying excessively."

Table IX indicates the extent of the emotional disturbance after visiting time. It will be seen that even in the 10–14-year-olds, a third of the children (32%) showed some disturbances after one or more of the visits. The younger the child, the more likely he was to be upset after departure of the visitors. 70·5% of those aged 5–6 and 86·3% of those aged 1–2 were disturbed after one or more visits. In the older age-group (10–14 years) the affected children were upset after approximately 1 in 5 of the visits (20·7%), whereas the 1–2-year-olds were upset after 3 out of 4 visits—76·9%. To put it in another way, the 8 affected 10–14-year-old children were disturbed on a total of 17 visiting days: the 38 1–2-year-olds were affected on a total of 186 visiting days—a much higher proportion.

As one would expect, far more of the younger children showed their feelings by crying than did older children. 72·6% of the 1–2-year-olds responded by crying, and 27·4% by merely looking miserable: 52·2% of the 5–6-year-olds responded by crying, and 5·9% of the 10–14-year-olds. It will be seen that there was much more overt crying after the departure of visitors than there was during the day.

Table X was designed to show whether the emotional disturbance was confined to the first few days or not. The table shows the proportion of children in the various age-groups who were disturbed during the day and after visiting in each of the first 3 four-day periods—i.e., in the first twelve days after admission to hospital. It will be seen that whereas in the older age-group only a small proportion of children showed any disturbance after the first four days, a very high proportion of the younger children continued to be affected after several days in hospital, and in fact were disturbed just as much in the third four-day period as in the first. For instance, of the 10–14-year-old children, 25·9% were upset after one or more visits in the first four days, as compared with 8·2% in the third four days, and the frequency of disturbance within the third four-day period was trivial, averaging a tenth of a day per child. The figures show that the incidence of emotional upsets rapidly fell off in all children of 5 years or older after the first four-day period. In the case of the 1–2-year-olds and the 3–4-year-olds, however, there was no falling off in the frequency of upsets as the days went by. Of the 3–4-year-olds, 68·7% were upset after visits in the first four-day period, as compared with 70·0% in the third period. The corresponding figures for the 1–2-year-olds were 82·2% and 100%. Furthermore, the 1–2-year-olds were upset on an average of 3 out of 4 visiting days in the third four-day period. In other words, they did not settle down as the days went by. They were better during the day, but during the day a third (31·2%) were still disturbed between the ninth and twelfth days.

TABLE X—INCIDENCE OF EMOTIONAL DISTURBANCE IN THE FIRST THREE FOUR-DAY PERIODS AFTER ADMISSION

| Age (yr.) | First 4 days | | Second 4 days | | Third 4 days | |
|---|---|---|---|---|---|---|
| | Showing emotional disturbance | Average no. of days in which disturbance occurred | Showing emotional disturbance | Average no. of days in which disturbance occurred | Showing emotional disturbance | Average no. of days in which disturbance occurred |
| 1–2 | | | | | | |
| During day | 68·9% | 2·2 | 41·9% | 1·0 | 31·2% | 0·9 |
| After visits | 82·2% | 2·9 | 74·9% | 2·2 | 100% | 3·1 |
| 3–4 | | | | | | |
| During day | 54·6% | 1·2 | 26·9% | 0·8 | 16·8% | 0·2 |
| After visits | 68·7% | 2·1 | 46·1% | 1·6 | 70·0% | 1·6 |
| 5–6 | | | | | | |
| During day | 38·6% | 0·8 | 20·5% | 0·4 | 8·3% | 0·1 |
| After visits | 63·6% | 1·1 | 33·3% | 0·7 | 13·6% | 0·4 |
| 7–9 | | | | | | |
| During day | 33·0% | 0·6 | 10·7% | 0·1 | 5·3% | 0·2 |
| After visits | 36·1% | 0·7 | 14·3% | 0·2 | 9·3% | 0·2 |
| 10–14 | | | | | | |
| During day | 22·2% | 0·3 | 9·1% | 0·1 | 5·1% | 0·1 |
| After visits | 25·9% | 0·5 | 5·9% | 0·2 | 8·2% | 0·1 |

The first column in each case shows the percentage of children in each age-group who showed emotional disturbance. The second column in each case was calculated by determining the number of days at risk for each child, and then calculating the proportion of such days on which emotional disturbances occurred—e.g., if a child stayed in hospital for only 7 days, the number of days at risk in the first 4-day period would be 4, as compared with 3 in the next 4-day period; if a child was only visited twice in the first 4-day period, the number of days at risk would be 2. Having determined this proportion, the average number of days' disturbance in each 4-day period was calculated for the group of children showing disturbances.

The duration of disturbance after departure of visitors can be only partially assessed. In 58% of the 427 days on which disturbance occurred after visiting, the child had settled when observed again half an hour after the visitors left. In 40·5% the child was still upset at that time. The remaining children seemed to be settled immediately after departure of the parents, but disturbed thirty minutes after. The proportion was the same in all age-groups, and has not, therefore, been tabulated.

A further analysis was made to determine whether there was more disturbance after the departure of the mother than after that of other visitors. Disturbance occurred after 28·8% of 781 visits of the mother alone, 27·5% of visits by the father alone, 33·7% of visits by the mother and father, and 61·7% of the 47 visits by the grandparents. The difference between the effect of visiting by the parents and the grandparents is of statistical significance. The reason for this odd finding is obscure. It did not seem to be related to a different age-distribution in the children visited by the grandparents as compared with those visited by the others.

We did not set out to determine whether children on days when they did not have a visitor were upset when other children did. We know that about a third (32·8%) of children were upset at visiting-time on a total of 22·1% of the 172 days on which they did not receive visitors: but we cannot say whether more of the children were upset when they did not receive visitors, because the records may be incomplete.

## Discussion

The important facts which this study has brought out are the remarkable faithfulness of parents in visiting their children as much as they possibly can, however costly it is in time and money; and the frequency with which children of all ages, but particularly the younger children, show emotional disturbances when separated from their parents. The study also casts light on the immediate after-effects of visiting, and the different sorts of response shown by children of various ages. The few responses which we have described correspond exactly to those recorded by Robertson and Bowlby (1952).

Inevitably, many questions are left unanswered. For instance, it is impossible to define the sort of child who was more likely to be upset than others. One would naturally expect that the wiser the management of the child before admission becomes necessary, the more he is loved, and the greater his sense of security, the less would he be disturbed by admission to hospital and the shorter-lasting would any harmful effects be. We cannot say

how those children who were most disturbed in hospital behaved at home. For all we know, they may have been crying constantly at home. We cannot estimate the feeling of security experienced at home by those children who were most upset when their parents left them at visiting-time. As we stated in our introductory remarks, the difficulties in an investigation like this are great. All we have done is to present our observations, and their interpretation is a matter of opinion. It is certainly clear that a high proportion of young children experience emotional disturbance in hospital, and it behoves us to do everything possible to reduce that disturbance to a minimum. This is a big subject, which we cannot discuss in detail here, but certain points seem to us to be of particular importance.

*Avoidance of Admission*

Young children should not be admitted to hospital unless it is absolutely necessary. Of the last 229 "new cases" referred to the professorial unit in the Children's Hospital at Sheffield, only 3% were admitted.

*Preparation for Hospital*

Children should be told, if possible, that they are going to be admitted to hospital and they should be given some idea of the experiences which they will meet. The Children's Hospital for the East Bay, California, issues a little booklet for the purpose, with illustrations designed to give the child some idea of what the hospital will be like.

*The Rôle of the Mother*

Where possible the mother should be admitted with her small child, to share a bedroom. Every hospital with a children's unit should have such accommodation. Often, of course, domestic circumstances will not allow the admission of the mother. Such an arrangement is particularly important for the young child who is going to be seriously disturbed by separation from his mother at the very time that he most needs her, when he is ill; and it is a great help to the mother who is particularly closely attached to her child, avoiding the trauma of separation and giving her the satisfaction of taking an active part in bringing about the child's recovery. We have such accommodation at Sheffield. The Babies' Hospital at Newcastle, which has similar facilities, is well known.

If domestic circumstances prevent the mother staying the night with her child, the next best thing is for her to spend the day with her child, taking a large share in nursing him, giving him his meals, attending to his toilet needs, and so on. If she cannot spend the whole day, she may be able to spend at least part of the day with him. If the mother cannot come in during the day, the next best thing is daily visiting.

It may be argued that the high incidence of emotional disturbance in young children on departure of the parents is a powerful argument against daily visiting. We cannot agree with that suggestion, for it seems reasonable to do everything one can to maintain the mother-child relationship. It is surely better for a child to see his mother every day—an event to which he very soon learns to look forward—even though he will be very sorry when she has to go, than to allow the child to pine for her every day, gradually becoming more and more convinced that she has deserted him, and perhaps that he is being punished, finally forgetting her and thus breaking the mother-child relationship, the strongest tie in his young life.

In any case it is surely the right of parents to see their children daily when they are ill. There is no doubt at all that parents greatly appreciate the right to visit their children daily, and our data show that the great majority of parents are deterred from visiting neither by the time nor cost involved, even when these are considerable. We find, too, that the doctors and nurses welcome daily visiting because it gives them much more contact with the parents, and therefore understanding of their children, and gives the parents much more opportunity to discuss their children's progress with those in charge of them, so that they lose much of their anxiety, if progress is satisfactory, and gain confidence in the hospital.

*Hospital Design*

Much more thought is required about the general design and decoration of children's hospitals. Certain modern outpatient departments may be efficient and easy to run, but they are distinctly forbidding and totally unattractive to the child. The child likes bright colours and attractive pictures, and there is no great difficulty in supplying these.

Cubicles are desirable for babies, but they should be used for toddlers and older children only when it is essential to prevent the spread of a specific infection. One of us recently visited a new wing of a famous Continental children's hospital, and was proudly shown the inpatient arrangements. Every child, up to the age of 14, was in a separate cubicle. One must balance the risk of cross-infection, which anyway is only partially prevented by the use of cubicles, against the psychological trauma of solitary confinement.

Ideally a child who is not too ill should be admitted to a playroom attached to the ward, where the sight of cheerful toys will help him to lose his tension. An attractive playroom-cum-dining-room should be a part of every ward.

*Admission Procedure*

The mother should be allowed to accompany the child to the ward, see him into bed, and sit with him for a time until he has become at least in part accustomed to his surroundings. Contrary to the opinion of many, we think that it is a good thing for the mother to be with her child when he is coming round from an anæsthetic.

At the Sheffield Children's Hospital we give all parents a leaflet, telling them, among other things, of the importance of visiting the child every day, and of using the visiting-time to the best advantage by reading to him, giving him his supper, and perhaps brushing his teeth, and tucking him up in bed for the night. They are warned not to promise to take him home unless what they say is true. They are reminded to give him his favourite teddy and toys and to send him letters and cards so that he does not feel that he is forgotten.

*Occupational Therapy*

A child who is well enough to appreciate them should be given suitable toys or books as soon as he comes in. The tendency is to delay giving them until he cries, or looks bored. The ward should have plenty of toys and books, especially for the younger children. Often the toys and books are for older children, and there is nothing for the younger ones. Moreover, toys tend to be too mechanical; educational toys * are of much greater value, in that they occupy the child for much longer periods and he enjoys them much more. The toys suitable for children of different ages have been discussed in detail elsewhere (Illingworth and Illingworth 1954). It is the doctor's responsibility to see that there is a supply of such toys in every ward and that they are issued. It is important that nurses should realise that a children's ward need not always be tidy.

An occupational therapist is of much value in a children's hospital. She, in turn, teaches the nurses who are attached to her for a period of their training.

Older children gain greatly from ward teaching. They thoroughly enjoy it, and it is excellent occupational therapy. In addition it serves to minimise psychological

* Such as those made by E. J. Arnold & Co., of Leeds, Philip & Tacey Ltd., Charles & Son, Educational Supply Association, and Wilkane Ltd.

disturbances when the child returns to school, for otherwise he may find that he has dropped a long way behind his fellows.

Voluntary workers have an important part to play. They keep the children occupied, read to them, and befriend them.

*Instruction of Nurses and Students*

This instruction should include the psychological features of the normal child and his development, the special problems of the sick child, and the effect of emotional deprivation and of separation from the mother, including the different types of response shown by children. In particular nurses need to know that the young child who is seriously disturbed by separation from his parents, crying excessively, and failing to coöperate, is not "naughty" or "spoiled," but is reacting normally, and needs all the love that can be given to him. It is wrong to devote spare time in the ward to the happy smiling child, and to ignore the one who needs attention most—the miserable, crying uncoöperative child who misses his mother so severely.

Nurses and students must understand the importance of striking a balance between the risks of cross-infection and psychological trauma, so that they will pick the child up and give him love when he most needs it. Other points requiring emphasis are the danger of talking in front of the child about his treatment and prognosis: the importance of never telling him a lie about procedures being painless when in fact they are painful, or about his going home when it is untrue, but of trying at all times to explain to a child exactly what is going to be done. The importance of premedication before anæsthetics must be emphasised. The child must not be allowed to see other children suffering, having mechanical procedures, such as lumbar puncture, carried out, or recovering from operations, such as tonsillectomy. In the Children's Hospital at Sheffield all nurses and students receive such instruction. They are all shown the film *A Two-year-old Goes to Hospital*, made by members of the Tavistock Clinic. Nurses are given a lecture-demonstration on Toys and Play. Students take part in debates on the ethics of research involving children, and on the avoidance of admitting children to hospital.

*Responsibility of the Doctor*

It is the doctor's responsibility to see that children are never kept in bed unnecessarily: that they are kept occupied: that their emotional needs are attended to, as far as possible; that the food which they are given is attractive: and that the duration of their stay is kept down to an absolute minimum. We are confident that much could be done in many children's units to reduce the duration of stay in hospital, and that a conscious effort should be made to do this. As an example of what can be done, a colleague at the Children's Hospital, Sheffield, Mr. R. B. Zachary, admits his patients with inguinal hernia in the morning, operates on them in the afternoon, and discharges them home on the following morning.

Finally, when the child is about to be discharged, the doctor can do much to ensure that the parents' attitude to their child on his return home will be a healthy one, that they will not "spoil" him, and that they will have some understanding of problems which may arise as a result of his experiences.

Though it is clear that separation from the mother is a disturbing experience to the child, we must preserve a sense of balance. We have no evidence that the child suffers anything but a temporary disturbance by his hospital experience, and it would certainly be disastrous if family doctors, conscious of the psychological trauma which may befall a child if he is taken into hospital, allowed him to suffer serious physical harm by not allowing him to have specialised investigation and treatment which can only be given in hospitals. Much can be done, by effective treatment in the home, and by an efficient outpatient department, to keep children out of hospital; but some have to be admitted, and it is the responsibility of all those responsible for his care to ensure that his stay in hospital is as happy as it can be, and that psychological trauma is reduced to a minimum.

## Summary

(1) We made a planned study of the behaviour of children in hospital, of the cost of visits by relatives, and of the reaction of children to the departure of their visitors. The study covered 181 children, and followed a pilot survey of 100 children.

(2) 50·6% of the children aged 1–4 years stayed in hospital 7 days or less.

(3) 90·6% of the maximum possible number of visits were made in the fourteen-day observation period—that is, less than 1 in every 10 chances for a visit was not accepted by a visitor of some kind.

(4) The average cost of each round journey by a visitor was 2*s.* 1*d.* 15·1% of all visits cost 4*s.* or more each. The average travelling time involved in each visit was 1¾ hours. 16% of all visits occupied 3 hours or more in travelling time. In spite of the high cost in money and time, strikingly few parents were deterred from frequently visiting their children. They made 74·1% of all visits costing 5*s.* or more, and 76·5% of all visits occupying 4 hours or more in travelling time.

(5) The mother visited in 73% of cases, and the father in 34·1% of cases, alone or with another.

(6) 32·4% of the children aged 1–4, 56·8% of those aged 5–6, and 72·4% of those aged 7–14 appeared to be emotionally normal during the observation period. Only 13·9% of those aged 1–4, 29·5% of those aged 5–6, and 62·1% of those aged 7–14 appeared to be undisturbed throughout the observation period *on departure of the visitors*. As expected, the older children showed their emotional disturbance mainly by subdued behaviour and by their facial expression, while the younger children cried, especially when their parents departed. In children of 5 years and over the emotional disturbance following visits grew much less frequent after the first few days, but in the younger ones it persisted or became even more striking as the days went by. We emphasise that we have no information about the behaviour of those children at home, so far as the amount of crying is concerned.

(7) We are strongly in favour of daily visiting, because it helps to preserve the mother-child relationship. It is far better for the child to see his mother every day, even though he will be upset when she has to leave him, than to allow him to become more and more certain that she has deserted him, and finally to forget her altogether.

(8) It is important to do everything possible to reduce psychological trauma to children in hospital, and we have outlined practical steps, based on experience at the Sheffield Children's Hospital.

(9) The wiser the management at home, the more secure the child is, and the less likely is he to suffer harm from admission to hospital; and a short stay in hospital is unlikely to have any but a very temporary disturbing influence on a mentally healthy normal child.

Our thanks are due to Dr. F. Lees, senior resident, and to our house-physicians Dr. H. P. Lambert, Dr. G. Forrest, Dr. L. H. Mofflin, and Dr. G. L. Asherson, and to Sister F. M. Watson, Sister J. L. Isaacs, Sister M. Jones, and Sister L. E. Shardlow, for keeping accurate daily records for the investigation. We also wish to thank Dr. G. H. Jowett and Miss W. Gibson, for advice about the statistics, and Mr. R. B. Zachary for kindly reading and criticising the paper.

### REFERENCES

Bowlby, J. (1951) *Bull. Wld Hlth Org.* monograph no. 2.
Capes, M. (1955) *Ibid*, **12**, 427.
Edelston, H. (1943) *Genet. Psychol. Monogr.* **28**, 3.
Illingworth, R. S., Illingworth, C. M. (1954) Babies and Young Children. London.
Prugh, D. G., Staub, E. M., Sands, H. H., Kirschbaum, R. M., Lenihan, E. A. (1953) *Amer. J. Orthopsychiat.* **23**, 70.
Robertson, J., Bowlby, B. (1952) *Courrier, Centre Enfance*, **3**, 131.

# VASCULAR OBSTRUCTION IN CHRONIC PYELONEPHRITIC KIDNEYS AND ITS RELATION TO HYPERTENSION

PRISCILLA KINCAID-SMITH
B.Sc., M.B. Witw'srand, D.C.P.
REGISTRAR IN PATHOLOGY,
POSTGRADUATE MEDICAL SCHOOL OF LONDON

THE typical histological features of chronic pyelonephritis have been described by Löhlein (1917), Staemmler and Dopheide (1930), Fahr (1938), and Weiss and Parker (1939).

I present here a new concept of the pathogenesis of chronic pyelonephritis and suggest a mechanism for the production of hypertension in this condition. It is postulated that vascular occlusion producing multiple ischæmic areas is largely responsible for the contracted pyelonephritic kidney. These areas show the incomplete or partial infarction (*Teilinfarzierung*) described by Fahr (1934): crowded glomeruli separated by shrunken tubules. The association between hypertension and obstruction of the renal arterial system is well known (Fishberg 1954, Pickering 1955). On the basis of the present observations it is suggested that the same mechanism explains the development of hypertension in some cases of chronic pyelonephritis.

## Observations

### CHRONIC AND HEALED PYELONEPHRITIS WITH ASSOCIATED HYPERTENSION

10 cases of malignant hypertension, in which irregularly scarred pyelonephritic kidneys were found at necropsy, form the material for this part of the study. The clinical diagnosis of malignant hypertension was only accepted in the presence of hypertensive retinitis with papillœdema. Cellular intimal hyperplasia in small arteries and fibrinoid necrosis in arterioles in the kidneys and other organs established the pathological diagnosis. The classical macroscopic and microscopic appearances of chronic pyelonephritis were present in all 10 cases. In 6 of these the disease was confined to one kidney. No obvious urinary obstruction was found at necropsy. Further particulars are given in table I.

*Vascular Lesions*

The arterial lesions were most commonly found in interlobar and arcuate arteries. They were also seen in interlobular arteries.

The external elastic lamina sometimes showed very gross thickening. Numerous abrupt and irregular interruptions were seen in both internal and external elastic laminæ; they were more numerous in the latter (fig. 1).

TABLE I—PYELONEPHRITIS AND HYPERTENSION

| Case no. | Age (yr.) | Sex | Kidney weights (g.) | | Macroscopic description of kidney (abstracted from records) |
|---|---|---|---|---|---|
| | | | Right | Left | |
| *Unilateral pyelonephritis:* | | | | | |
| 1 | 59 | F | 200 | 50 | Left kidney: coarse irregular scarring |
| 2 | 22 | F | 70 | 165 | Right kidney: irregular scarring, shrunken lower pole, no obstruction in artery to lower pole |
| 3 | 27 | F | "Half normal" | "Normal" | Right kidney: irregular scarring and contraction |
| 4 | 43 | F | 90 | 190 | Right kidney: irregular areas of cortical atrophy |
| 5 | 15 | F | "40 mm. in length" | 180 | Right kidney very small and scarred |
| 6 | 50 | F | 150 | 70 | Left kidney shrunken and "pyelonephritic," with calculi in pelvis |
| *Bilateral pyelonephritis:* | | | | | |
| 7 | 25 | F | 72 | 40 | Irregular scarring and shallow cortical depressions of both kidneys |
| 8 | 23 | F | 46 | Not recorded | Irregular scarring and cortical atrophy of both kidneys |
| 9 | 47 | F | 110 | 85 | Irregular scarring of both kidneys; atrophy of lower third of left kidney with no occlusion in the artery to this area |
| 10 | 45 | M | 127 | 125 | Irregular scarring of both kidneys |

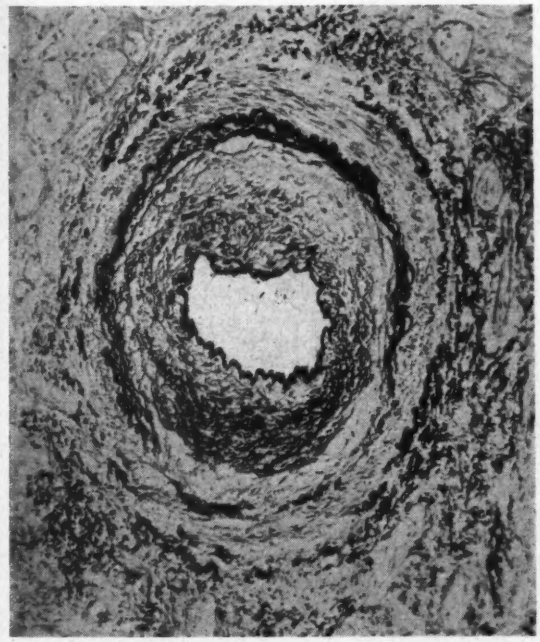


Fig. 1—Arcuate artery showing irregular destruction of internal and external elastic laminæ, especially of the latter. Intima shows fibrocellular hyperplasia with narrowing of lumen. (Weigert's elastic and neutral red. × 90.)

The elastic laminæ were often corrugated (figs. 2 and 3). Not uncommonly all that remained of an artery was a cylinder of coiled elastic fibres, the place of the remainder of the vessel having been completely taken by collagen. Fibrous tissue often took the place of the medial muscle at the same site as the destructive lesions in the elastic laminæ (fig. 4).

The changes in the intima were very striking and extended beyond the areas where definite destruction of the media could be demonstrated. They were invariably

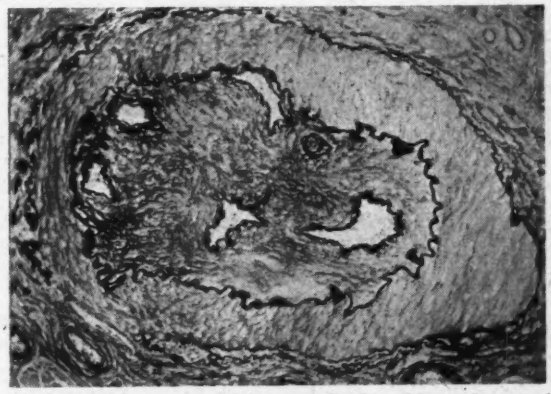


Fig. 2—Interlobar artery showing recanalisation of lumen by several separate channels, corrugation of internal elastic lamina, and areas of interruption of external elastic lamina. (Weigert's elastic and neutral red. × 91.)

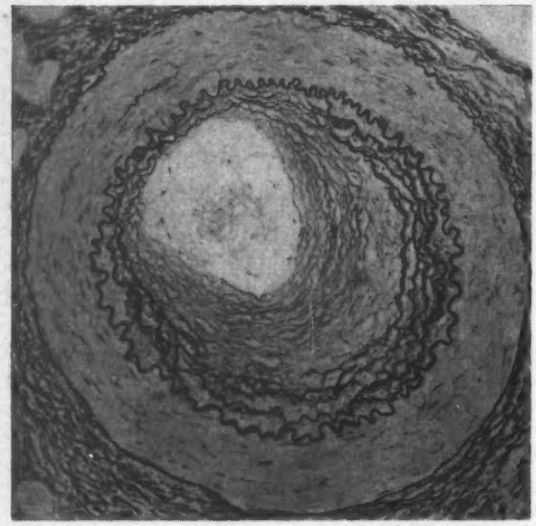


Fig. 3—Interlobar artery showing lunate (eccentric) intimal thickening and corrugation of internal elastic lamina. (Weigert's elastic and van Gieson. × 47.)

Fig. 5—Interlobar artery showing extreme narrowing of lumen by fibrocellular intimal proliferation. (Weigert's elastic and van Gieson. × 43.)

present throughout an area of scarring but were far less noticeable in relatively normal areas of cortex. Since, however, each patient had had severe hypertension, no entirely normal vessels were observed. The usual lesion was a fibrocellular intimal proliferation in which fine collagen and elastic fibres were present (figs. 1–5). Extreme narrowing of the lumen was common (fig. 5), but complete occlusion was not. A lunate intimal proliferation (fig. 3), similar to that described by Doniach (1949) in tuberculous meningitis, was seen in a few arteries. Dense hyaline collagen, devoid of cells and elastic fibres, sometimes obstructed the lumen at the site of severe destruction of the media. In several instances the picture was identical with that seen in recanalisation following thrombosis (Wright 1954); here two or three separate vascular channels were present, each with a newly formed internal elastic lamina (fig. 2).

Fig. 4—Arcuate artery showing destruction of media (muscle and elastic) and intimal proliferation. The area of cortex supplied by this vessel is shown in fig. 6. (Weigert's elastic and van Gieson. × 40.)

*Lesions of Renal Parenchyma*

The parenchymal lesions in chronic pyelonephritis are subdivided below into (1) those following ischæmia and (2) thyroid-like areas in which acute inflammation is thought to be an important causal factor. Although the two pictures described are often clearly distinct, various combinations of the two may be seen.

*Lesions following ischæmia.*—Serial sections showed that arteries with severe lesions like those described above often supplied contracted and sharply demarcated areas of renal cortex (fig. 6). The size of the area varied with the size of the artery involved, the larger ones corresponding to broad shallow U-shaped depressions seen macroscopically. In these areas it was possible to trace a gradation from purely ischæmic lesions to classical chronic pyelonephritic lesions (figs. 7–9). Ischæmic areas with no superimposed inflammation were uncommon and resembled the incomplete infarcts described by Fahr (1934), showing small nephrons with glomerular crowding due to tubular atrophy. The atrophic tubules had small lumina lined by cuboidal epithelium (fig. 7). Inflammatory changes superimposed on this picture, consisting of periglomerular fibrosis and cellular infiltration (fig. 8), produce the classical stage I of chronic pyelonephritis (Staemmler and Dopheide 1930). A gradual transition is seen from this appearance to the well-recognised pyelonephritic lesion in which the glomeruli show partial or complete hyalinisation and the tubules show further atrophy and contain small colloid casts (fig. 9) as in stage II of Staemmler and Dopheide. These observations suggest that the three pictures described are stages in the

Fig. 6—Sharply demarcated contracted area of renal cortex, showing shallow depression of surface and incomplete infarction with mild superimposed inflammatory changes. Damaged vessel supplying this area of cortex is in bottom left-hand corner. Fig. 4 shows another level of same vessel. (Hæmatoxylin and eosin. × 8.)

process of this type of pyelonephritic scarring and that ischæmia is the primary factor in this process.

*Thyroid-like areas.*—A different appearance, also characteristic of chronic pyelonephritis, is that seen in the thyroid-like areas (fig. 10): dilated tubules with a flat epithelium are filled with colloid, and glomeruli are represented by scanty hyaline scars. This appearance corresponds to stage III of Staemmler and Dopheide (1930), who regard it as a progression from stage II. Present observations, however, suggest that the thyroid-like areas result rather from acute inflammation of the renal parenchyma, with consequent destruction of most of the nephrons and persistence of colloid-filled tubules and occasional glomerular scars.

### COMPARISON OF LESIONS IN HYPERTENSIVE AND NORMOTENSIVE PATIENTS WITH CHRONIC PYELONEPHRITIS

Of 45 consecutive patients with chronic pyelonephritis examined at necropsy in this department during the past ten years 30 (66·6%) were hypertensive and 15 (33·3%) normotensive. The hypertensive patients usually had severe renal contraction and extensive pyelonephritic scarring, whereas the kidneys in the normotensive group were often of normal size with only occasional pyelonephritic scars. Histologically the hypertensive patients had numerous lesions of the type described above as following ischæmia—areas of incomplete infarction and of stages I and II of Staemmler and Dopheide. In the non-hypertensive kidneys these lesions were rarely seen. There was no significant difference in the extent of thyroid-like areas in the two groups. The extent of the ischæmic lesions in hypertensive and normotensive patients is summarised in table II.

### LESIONS IN ACUTE PYELONEPHRITIS

The nature of the arterial lesions observed in chronic pyelonephritis suggested that they resulted from inflammation. This prompted the study of 50 post-mortem kidneys showing acute pyelonephritis with a view to finding arterial lesions in the acute stage.

*Vascular Lesions*

In cases where intense acute inflammation involved an artery, a heavy polymorph infiltration of the arterial wall was accompanied by destruction of muscle and elastic tissue (fig. 11). This type of lesion was occasionally associated with secondary thrombosis in the vessel, the thrombus being adherent to the areas of most destruction.

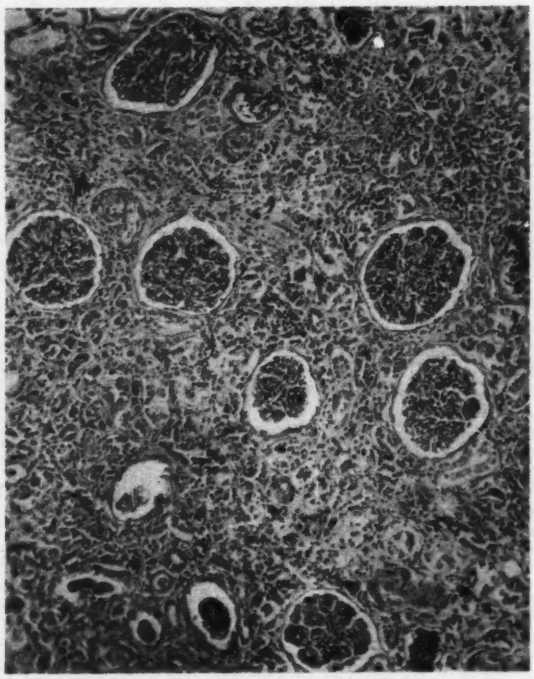


Fig. 7—Area of incomplete infarction showing crowded glomeruli and atrophic tubules without inflammatory changes. (Hæmatoxylin and eosin. × 90.)

Fig. 8—Ischæmic area showing incomplete infarction with superimposed inflammatory changes, periglomerular fibrosis, and cellular infiltration. Atrophic tubules still present (Staemmler and Dopheide stage I). (Hæmatoxylin and van Gieson. × 90.)

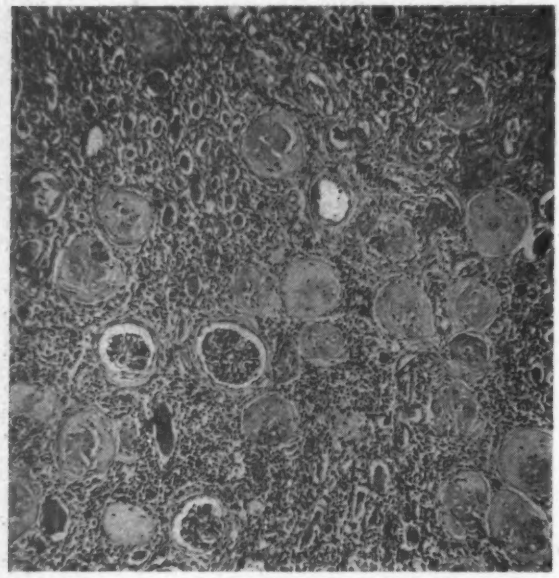


Fig. 9—Ischæmic area showing periglomerular fibrosis and hyalinisation of glomeruli, inflammatory infiltration, and colloid casts in small atrophic tubules. (Staemmler and Dopheide stage II) (Hæmatoxylin and eosin. × 73.)

Minor degrees of inflammatory destruction involving only the outer part of the arterial wall were common.

Inflammatory endarteritis was common but usually produced far less narrowing of the lumen than that seen in chronic cases. The amount of endarteritis was proportional to the intensity of the inflammation involving the vessel wall and surrounding tissue. The endarteritis consisted of loosely arranged elongated cells apparently arising from the endothelium (fig. 12). Occasional polymorphs were present among the proliferated endothelial-cells. This intimal proliferation differed from that described in chronic pyelonephritis in its loose arrangement and in the paucity of collagen and elastic fibres.

*Parenchymal Lesions*

No areas of incomplete infarction were seen in acute pyelonephritis except where the acute inflammation was superimposed on a chronic lesion. Occasionally complete infarction was observed, however, resulting from inflammatory arterial thrombosis. Where inflammatory destruction of tubules caused glomerular crowding, a superficial resemblance to incomplete infarction was noted. The two conditions could usually be distinguished, however, by the presence of small atrophic tubules between the glomeruli in the ischæmic areas, whereas in those resulting purely from inflammation the glomeruli were separated by granulation tissue.

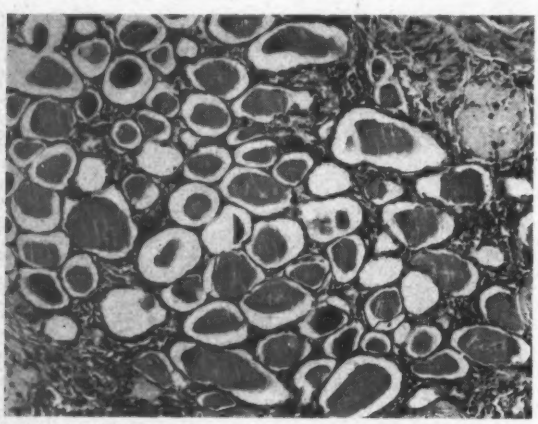


Fig. 10—Thyroid-like collections of tubules showing flattened epithelium and containing colloid casts. A few hyaline glomerular scars are present. (Hæmatoxylin and eosin. × 100.)

## Comment on Observations

This study of the lesions in acute and chronic pyelonephritis indicates that, when the arteries are involved in the inflammation, destructive lesions of the wall appear with accompanying complete occlusion or extreme narrowing by inflammatory endarteritis. There may or may not be associated thrombosis. The greater degree of intimal proliferation observed in chronic cases suggests that this process continues as long as active inflammation is present in the kidney.

Vascular lesions identical with those described above have not been observed in kidneys other than those showing pyelonephritis. In healed polyarteritis nodosa the arterial lesions may be very similar and the damaged vessels supply cortical areas of incomplete infarction. In this condition, however, superimposed inflammation is not usually seen in the ischæmic renal parenchyma, and because of other well-known distinctive features confusion with pyelonephritis should not arise.

It has been mentioned that parenchymal lesions resembling areas of incomplete infarction were found in the cortex supplied by the narrowed or occluded vessels in chronic pyelonephritis. These areas were often wedge-shaped, and their superficial surfaces showed broad shallow depressions, said to be characteristic of pyelonephritic scars (Weiss and Parker 1939, Raaschou 1948, Allen 1951). The ischæmic areas are likely to be more susceptible to further involvement by inflammation. They often show distinct infiltration by lymphocytes and plasma-cells but retain small atrophic tubules which distinguish them from areas of glomerular crowding resulting from inflammatory destruction of tubules. The sharp border often seen between an area of chronic pyelonephritic scarring and normal renal parenchyma could be explained on the basis of inflammation limited to an ischæmic area. A similar explanation may apply to the sharply defined wedges of inflammatory infiltration mentioned by Allen (1951) in his description of subacute pyelonephritis.

TABLE II—ISCHÆMIC LESIONS IN HYPERTENSIVES AND NORMOTENSIVES

| Extent of ischæmic lesions* | Hypertensive group (30 cases) | Normotensive group (15 cases) |
|---|---|---|
| Severe .. .. | 24 cases (80%) including 6 cases of malignant hypertension | 1 case (6·6%) |
| Moderate .. | 2 cases (6·6%) | 2 cases (13·3%) |
| Slight .. .. | 4 cases (13·3%) | 12 cases (80%) |

* This term includes areas of incomplete infarction and Staemmler and Dopheide's (1930) stages I and II of pyelonephritis.

Observations in this series support the view of Mallory et al. (1940) that thyroid-like areas result from the distension of tubules with polymorphs. Staemmler and Dopheide (1930) postulated that stage-II pyelonephritis progressed to thyroid-like areas (their stage III). However, it is difficult to appreciate how the large distended tubules of thyroid-like areas could develop from the small atrophic tubules of stage II of Staemmler and Dopheide. The small colloid-filled tubules scattered through areas of stage-II pyelonephritic scars (fig. 9) are probably their counterpart. I suggest that thyroid-like areas result from acute inflammation of renal parenchyma,

Fig. 11—Interlobar artery in acute pyelonephritis showing cellular infiltration, destruction of medial muscle and elastic, and secondary thrombosis. (Weigert's elastic and van Gieson. × 45.)

which may have been either normal or rendered ischæmic by the vascular lesions, but before definite contraction and tubular shrinkage have taken place. No relation of thyroid-like areas to hypertension was found in this study.

Observations in the 45 cases of chronic pyelonephritis showed that lesions differed in the hypertensive and non-hypertensive groups. Both the degree of renal contraction due to pyelonephritic scarring and the number of ischæmic areas were greater in the hypertensive cases. These results are, however, not entirely conclusive, because the small normotensive group did not include any patients with severely contracted pyelonephritic kidneys. Such cases have been reported by Longcope and Winkenwerder (1933) and Weiss and Parker (1939).

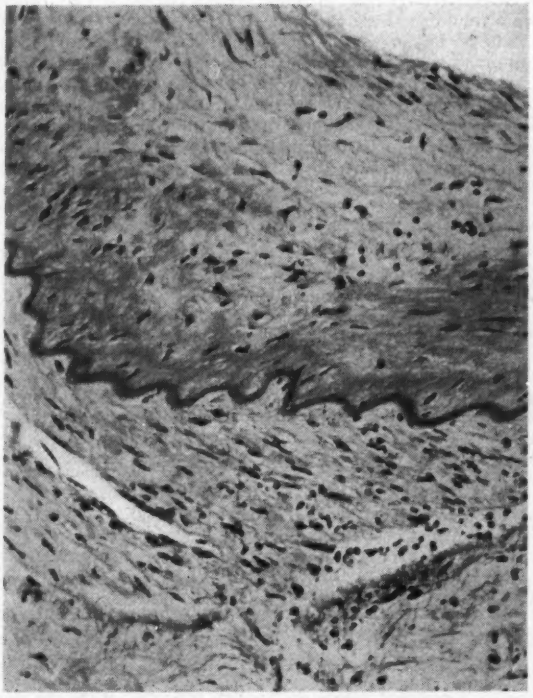


Fig. 12—Interlobar artery in acute pyelonephritis showing intimal hyperplasia, polymorph infiltration of wall, and interruption of external elastic lamina. (Hæmatoxylin and eosin. × 190.)

Only one such case was found in our records:

A woman, aged 32, came to necropsy with a five-year history of recurrent attacks of pyelonephritis. During the last two years of life the blood-urea level had been about 200 mg. per 100 ml., rising terminally to 650 mg. per 100 ml. The blood-pressure was 130/70 mm. Hg during most of the period of observation, but shortly before death it rose to 160/100 mm. Hg. At necropsy both kidneys (45 g. and 60 g.) showed gross contraction, fibrosis, irregular scarring, and adherent capsules. Microscopic sections of kidney from three different areas showed a few collections of grossly hypertrophied nephrons, but the remainder of the renal parenchyma had been completely replaced by thyroid-like areas devoid of glomeruli. Vascular changes were similar to those in hypertensive cases, but no areas of incomplete infarction or stages I and II of pyelonephritis (Staemmler and Dopheide 1930) were present.

It should be emphasised that, in the above-described case and in the few normotensive cases in this series with pyelonephritic renal contraction, arterial lesions were found which were similar to those described in hypertensive cases. The important difference lay in the parenchymal lesions. Incomplete infarction and stages I and II (Staemmler and Dopheide 1930) of pyelonephritic lesions were common in hypertensive cases and either minimal or absent in normotensive ones. Thyroid-like areas formed the main parenchymal lesion in contracted kidneys from normotensive cases, and since these were present in both groups their relation to hypertension was not apparent.

Where damaged vessels were present in normotensive cases they supplied thyroid-like areas. Therefore I suggest that ischæmic areas (incomplete infarcts and stages I and II of pyelonephritic lesions) are causally related to the development of hypertension in pyelonephritis. Where, however, parenchyma deprived of its blood-supply has been converted to a thyroid-like area by superimposed acute inflammation, no such relationship is maintained. In other words, hypertension in chronic pyelonephritis is associated with areas of ischæmic renal parenchyma which have escaped complete destruction or conversion to thyroid-like areas by acute inflammation.

## Discussion

### *Pathology of Chronic and Healed Pyelonephritis*

I have not been able to find in published reports any mention of the production of areas of incomplete infarction in chronic pyelonephritis. Kimmelstiel and Wilson (1936), commenting on the close resemblance between pyelonephritic scars and incomplete infarction, suggested that in the latter the finding of an old arterial thrombosis in the artery of supply would differentiate the two lesions. Weiss and Parker (1939) apply the same criterion for differentiating old infarcts from pyelonephritic scars. The macroscopic appearances of the kidneys in chronic pyelonephritis and in multiple old infarction may be identical (Weiss and Parker 1939, Raaschou 1948, Allen 1951). The present observations elucidate this macroscopic and microscopic resemblance by showing that arterial obstruction with or without thrombosis may result from pyelonephritis.

This study shows that broad shallow scars in pyelonephritis may result from arterial occlusion. I do not suggest that this is the only cause of pyelonephritic

TABLE III—AGE-DISTRIBUTION

| Type | No. of cases | Age (yr.) | |
|---|---|---|---|
| | | Range | Average |
| Malignant hypertension (clinically and pathologically) .. .. .. .. | 7 | 22–50 | 34 |
| Hypertension with diastolic B.P. over 110 mm. Hg but without clinical and pathological features of malignant hypertension .. .. .. .. | 14 | 40–83 | 57 |
| Hypertension with diastolic B.P. between 100–110 mm. Hg .. .. .. | 10 | 31–77 | 59 |
| Normotensive .. .. .. .. | 14 | 43–87 | 69 |

scarring, which can clearly also result from inflammatory destruction of renal parenchyma. Previous descriptions of the vascular changes in chronic pyelonephritis (Staemmler and Dopheide 1930, Linder 1937, Fahr 1938, Weiss and Parker 1939) have not, however, drawn attention to the importance of the obstructive arterial lesions in the pathogenesis of the contracted pyelonephritic kidney.

*Chronic Pyelonephritis and Hypertension*

In this series of 45 cases of chronic pyelonephritis all those which showed severe renal contraction due to pyelonephritic scarring were hypertensive. Heptinstall and Gorrill (1955) found, in experimental pyelonephritis in rabbits, hypertension only in association with severe renal scarring.

The age-distribution in the present series is shown in table III. Although this is a small series, these figures, taken in conjunction with the pathological findings, suggest that, particularly in the younger age-group, pyelonephritic contracted kidneys are often associated with hypertension. Only one young normotensive with grossly contracted pyelonephritic kidneys could be found in our records.

In an extensive review of the incidence of hypertension in pyelonephritis Smith (1948) cites figures varying from 9% to 47%. One of the highest figures cited was that of Braasch et al. (1940) in "atrophic pyelonephritis": in 1684 cases subjected to renal surgery they found hypertension in 18·6% of cases of "pyelonephritis other than atrophic" and 46·5% in "atrophic pyelonephritis." They state that "renal infection was not an etiologic factor in hypertension unless it caused widespread atrophic changes in the renal parenchyma."

The incidence of hypertension found by Weiss and Parker (1939) in chronic and healed pyelonephritis was 75%.

Longcope (1937) found hypertension in 10 of 15 patients with terminal chronic pyelonephritis.

The present figure of 66·6% for the incidence of hypertension in 45 cases of chronic pyelonephritis is in keeping with the latter two series. The incidence of hypertension in a pathological survey may differ from that in a clinical series for two reasons: a clinical attack of pyelonephritis may lead to insignificant renal scarring; and cases of hypertension associated with chronic pyelonephritis may have no clinically detectable features of the latter condition.

Weiss and Parker (1939) first suggested a causal relationship between the vascular changes in pyelonephritis and hypertension. They were concerned mainly with arteriolar changes which they called hyperplastic arteriolosclerosis. They concluded that hypertension in pyelonephritis depended on obliterative lesions of the renal arterioles.

The evidence presented here shows that a situation exists in chronic pyelonephritis which is analogous to that in renal vascular obstruction due to various causes known to be associated with hypertension.

Since Goldblatt et al. (1934) showed that hypertension followed experimental clamping of the renal artery, many reports have appeared of hypertension associated with renal ischæmia due to different processes: lesions of the main renal artery (Leadbetter and Burkland 1938, Howard et al. 1940, Perry 1945, Goodman 1952, Pickering 1955), embolism of renal vessels (Prinzmetal et al. 1942, Fishberg 1942), and ligature of an aberrant renal artery (Pickering and Heptinstall 1953).

Leiter (1938) reported a case of malignant hypertension associated with occlusion of multiple small renal arteries, producing a histological picture of alternating areas of normal and ischæmic renal parenchyma.

A similar microscopic appearance in the kidney is seen in polyarteritis nodosa (Russell 1929), which only causes hypertension when it involves the renal arteries (Fishberg 1954).

Among reports demonstrating the causal relationship between renal arterial obstruction and hypertension is that of Howard et al. (1954), removal of the ischæmic kidney in six cases relieving severe hypertension.

In many of the above-mentioned reports where histological details on the kidney are available the picture of incomplete infarction is described. Selye's (1950) endocrine kidney, which is deprived of most of its blood-supply by ligation of the aorta between the two renal arteries, a manœuvre producing malignant hypertension in rats, shows a somewhat similar picture of crowded glomeruli and atrophic proximal convoluted tubules. The occurrence of ischæmic areas in chronic pyelonephritis and their association with arterial obstruction suggest that they are causally related to the development of hypertension in this condition.

## Summary

Obstructive vascular lesions and associated ischæmic renal parenchymal lesions in hypertensive chronic pyelonephritis are described.

The renal parenchymal lesions in 45 consecutive necropsy cases of chronic pyelonephritis are compared, and differences between the hypertensive and normotensive cases are described.

Because the nature of the vascular lesions in cases of chronic pyelonephritis suggested that they were the result of inflammation, 50 necropsy kidneys showing acute pyelonephritis were studied. Destructive lesions of the arterial walls and obstructive lesions of the lumen were found in these cases.

These findings are discussed in relation to their importance both in the pathogenesis of contracted pyelonephritic kidneys and in the development of hypertension in pyelonephritis. Ischæmic parenchymal lesions such as are described here in chronic pyelonephritis are also found in other conditions in which renal vascular obstruction is known to be associated with hypertension. In view of this the ischæmic lesions are thought to be causally related to the development of hypertension in chronic pyelonephritis.

I am grateful to Prof. J. H. Dible, Prof. J. McMichael, Prof. C. V. Harrison, and Dr. I. Doniach for their advice and encouragement in the preparation of this paper; Mr. J. Griffin and his staff for the histological preparations; and Miss R. Klein for the photomicrographs.

## REFERENCES

Allen, A. C. (1951) The Kidney. New York.
Braasch, W. F., Walters, W., Hammer, H. J. (1940) *J. Amer. med. Ass.* **115**, 1837.
Doniach, I. (1949) *J. Path. Bact.* **61**, 253.
Fahr, T. (1934) *In* Henke, F., Lubarsch, O. Handbuch der speziellen pathologischen Anatomie und Histologie. Berlin; vol. VI, part 2.
— (1938) *Virchows Arch.* **301**, 140.
Fishberg, A. M. (1942) *J. Amer. med. Ass.* **119**, 551.
— (1954) Hypertension and Nephritis. 5th ed., London; p. 310.
Goldblatt, H., Lynch, J., Hanzal, R. F., Summerville, W. W. (1934) *J. exp. Med.* **59**, 347.
Goodman, H. L. (1952) *New Engl. J. Med.* **246**, 8.
Heptinstall, R. H., Gorrill, R. H. (1955) *J. Path. Bact.* **69**, 191.
Howard, J. E., Berthrong, M., Gould, D. M., Yendt, E. R. (1954) *Bull. Johns Hopk. Hosp.* **94**, 51.
Howard, T. L., Forbes, R. P., Lipscomb, W. R. (1940) *J. Urol.* **44**, 808.
Kimmelstiel, P., Wilson, C. (1936) *Amer. J. Path.* **12**, 45.
Leadbetter, W. F., Burkland, C. E. (1938) *J. Urol.* **39**, 611.
Leiter, L. (1938) *J. Amer. med. Ass.* **111**, 507.
Linder, F. (1937) *Frankfurt. Z. Path.* **51**, 150.
Löhlein, M. (1917) *Beitr. path. Anat.* **63**, 570.

*References continued at foot of next column*

# PERSISTENT FUNGUS INFECTIONS OF SKIN, HAIR, AND NAILS

A. J. E. BARLOW
M.D. Leeds
CONSULTANT DERMATOLOGIST,
HUDDERSFIELD ROYAL INFIRMARY, YORKS

F. W. CHATTAWAY
M.Sc., Ph.D. Lond.
LECTURER IN BIOCHEMISTRY IN THE UNIVERSITY OF LEEDS

ALTHOUGH many species of dermatophytes live on the human body without necessarily causing symptoms or signs, the same species may, without obvious reason, give rise to signs of clinical disease, which is normally localised to an area characteristic for the species and may spread to another person. Such infections may show very considerable variation in their natural course and in their response to treatment.

In spite of much effort to improve therapy the results are little, if at all, better than they were under treatment by the more old-fashioned methods. The two categories of infections which particularly illustrate this are: (1) tinea capitis due to the anthropophilic group of fungi, and (2) those due to *Trichophyton rubrum*.

Immediately after the 1939–45 war there was a world-wide epidemic of tinea capitis due to *Microsporum audouini* which focused attention on treatment by methods other than epilation by X rays. Claims were made for the effectiveness of many fungicides applied topically; but review of the results showed that no one method produced consistently more than 70% cure in any large series of cases.

Most observers noticed many inflammatory reactions, and appreciated that these constituted a non-specific reaction on the part of the host by which the infection was normally terminated. The results also suggested that, where the infection was cured without evident clinical inflammation, this might be due to some equivalent non-specific reaction rather than to destruction of the fungus by a topically applied fungicide.

The epidemic gradually came to an end about 1950. Hence, although we were able to report results of treatment in 261 cases observed in 1947–49 (Barlow et al. 1950), we saw only sporadic cases in 1949–51, since when we have not encountered a single case in the school population of Huddersfield. Other observers have had the same experience, and we find it difficult to believe that it is due to the effectiveness of our treatment but feel that it is more likely due to the natural waning of the epidemic, which has curtailed the spread of infection. Indeed, it is of particular interest that, although at the height of the epidemic we were able to obtain a cure-rate as high as 74%, the same local treatment was much less effective when used in a smaller series of sporadic cases.

We concluded that there must be considerable differences between epidemic and sporadic cases, the host-parasite relationship in epidemic cases normally being more unstable and the natural course of the disease therefore much shorter. This seems to explain the discrepancy between the findings of Kligman (1955) and those of many other observers on the chronicity of *M. audouini* infections. His beautifully controlled observations were made on an artificially induced epidemic; and, though this has shown in perfect detail the morphology of invasion of the skin and hair follicle by the fungus, one must be chary of assuming that natural infections involute in the way in which artificial infections apparently do. Indeed in his original report (Kligman 1952) he noted that among those children who acquired infection naturally "there were a significant number in whom spontaneous resolution did not occur even after two years. This is in contrast to the experimental series who had undoubtedly a lesser degree of susceptibility."

A greater understanding of the host-parasite relationship is, we feel, essential to the whole subject of fungus infections, for it is being increasingly appreciated that there may be very wide variations. Advances on these lines require a detailed knowledge of the formation, properties, and structure of keratin as well as of the biochemistry of the fungi concerned.

### Variations in Parasite

The dermatophytes form a large heterogeneous group, probably derived from soil fungi, which are very adaptable to parasitism on man and animals. From a clinical point of view two distinct groups seem to emerge: in one the main attack is on the hair follicle with the production of tinea capitis, tinea corporis, and tinea circinata; in the other the attack is essentially on the horny layer, possibly the nails, and only very rarely the hair follicle, as in tinea pedis.

Normally a species keeps to its particular pattern of attack, but it is being increasingly appreciated that there may be a very wide variation within a species, a factor which gave rise to the naming of 184 different species by 1934 (Gregory 1935). It is now recognised, however, that most of these are really variants of a much smaller number, and it is therefore not surprising that any species which may show such wide variation in artificial culture should show equally wide variation in parasitism.

Species which are normally parasitic on an animal have the ability to invade a hair follicle, and when they attack man they invade the follicles whether on smooth or hairy skin. Thus the zoophilic organisms *M. canis*, *T. discoides*, and *T. mentagrophytes*, in all of which the host-parasite relationship is unstable, invade the follicles and cause inflammation in man.

*T. mentagrophytes* seems occasionally able to adapt itself to man more completely, but in so doing it apparently loses the ability to invade the hair follicles and becomes the cause of tinea pedis, possibly with infection of the nails. Such infections, however, are not so persistent as those due to the anthropophilic *T. rubrum*, being more amenable to treatment and possibly resolving spontaneously more often. Sulzberger and Baer (1955) suggest that *T. mentagrophytes* may require "interspersed passages through an animal host to maintain its virulence." If this is so, one would expect it to reacquire its tendency to invade the follicle and therefore to produce follicular infection again in the human host. If these two forms are to be regarded as variants of *T. mentagrophytes* it would seem that the form giving rise to tinea pedis is an attenuated variant of the animal strain. This is supported by the work of Silva and Benham (1954), who showed that fungus isolated from tinea pedis and inoculated into a guineapig produced only transitory epidermal infection and did not invade the follicles as did strains isolated from a natural infection in a mouse.

No variants of this type seem to have been attributed to *T. discoides* or to *M. canis*, and the former may at least retain its virulence for its normal host after long

DR. KINCAID-SMITH: REFERENCES—*continued*

Longcope, W. T. (1937) *Ann. intern. Med.* **11**, 149.
— Winkenwerder, W. L. (1933) *Bull. Johns Hopk. Hosp.* **53**, 255.
Mallory, G. K., Crane, A. R., Edwards, J. E. (1940) *Arch. Path.* **30**, 330.
Perry, C. B. (1945) *Brit. Heart J.* **7**, 139.
Pickering, G. W. (1955) High Blood Pressure. London; p. 380.
— Heptinstall, R. H. (1953) *Quart. J. Med.* **22**, 1.
Prinzmetal, M., Hiatt, N., Tragerman, L. J. (1942) *J. Amer. med. Ass.* **118**, 44.
Raaschou, F. (1948) Studies of Chronic Pyelonephritis. Copenhagen.
Russell, D. S. (1929) *Spec. Rep. Ser. med. Res. Coun., Lond.* no. 142.
Selye, H. (1950) The Physiology and Pathology of Exposure to Stress. Montreal; p. 540.
Smith, H. W. (1948) *Amer. J. Med.* **4**, 724.
Staemmler, M., Dopheide, W. (1930) *Virchows Arch.* **277**, 713.
Weiss, S., Parker, F. jun. (1939) *Medicine, Baltimore*, **18**, 221.
Wright, G. P. (1954) An Introduction to Pathology. 2nd ed., London; p. 320.

periods in artificial culture. We have produced with a homogenate of a culture used for metabolic work in the laboratory for eight months characteristic lesions in a calf.

### Medium for Parasitic Growth

The host offers to the parasite, as a medium for growth, a thin sheet of soft keratin dipping down in the hair follicles to ensheathe a shaft of hard keratin and a keratogenous zone beneath. Growth of the fungus is for all practical purposes restricted to these structures, although the development of occasional granulomatous lesions in *T. rubrum* infections suggests that this fungus may invade the dermis.

Most observers state that the fungi can grow only in fully keratinised tissues, and that the keratogenous zone is never invaded. Unfortunately there are no accurate observations on this, and it is difficult to be dogmatic about the exact point at which hard keratinisation in the hair follicle is complete. In any case, the biochemical circumstances of the lower two-thirds of the follicle influence very much the growth of all those dermatophytes which invade it: (1) growth of the fungus is most persistent in this region, the epidermal infection dying out; (2) the method of invasion and sporulation is normally characteristic for a species; and (3) both species of microsporon and *T. schoenleini* produce fluorescent materials when growing there. This last characteristic has never been shown except in the lower two-thirds of the living follicle, and there is no record of its production in vitro. For years we have grown representative strains of the dermatophytes on keratin in vitro under different conditions in attempts to simulate the parasitic pattern of growth but always unsuccessfully. We feel that this pattern is probably related to keratinisation.

There is increasing evidence (Sulzberger and Baer 1955) that the dermatophytes can live saprophytically on the skin without producing any visible signs of their presence. Once, however, pathogenic invasion has taken place, the clinical picture is ascribable to two main factors: (1) damage to the fabric of the skin, hair, and nails which the fungus causes by its growth through it, including scaling, lustreless, and broken hair and nails; and (2) the host's reaction, including both epidermal and follicular inflammation as well as varying eczematous reactions and hyperkeratosis of the affected areas.

Inflammation essentially due to follicular infection and potentially curative is the rule with zoophilic fungi but may develop with any fungus which invades the follicles, and has been described in infection with most of the anthropophilic fungi.

Eczematous reactions, on the other hand, are not curative and develop essentially in infection with those organisms which give rise to tinea pedis.

Hyperkeratosis of the palm or sole, where corresponding nails are affected, is characteristic of *T. rubrum* infections and not only is not curative but also predisposes to chronicity, since it provides a medium in which the fungus may vegetate and through which topically applied fungicides cannot penetrate.

There is no exact knowledge of the factors which stimulate the host's reaction, but it has been suggested by Kligman (1955) that *M. audouini* may produce "an exotoxin which irritates the skin." This seems possible, but whether a specific toxin is elaborated by each dermatophyte or some common by-product of metabolism is produced to which the host may become sensitive remains open to question.

### Aspects of Treatment

Until recently the usual treatment, apart from epilation by X rays in tinea capitis, has been the topical application of fungicides. The uncertainty of the results, however, has caused the production of a wide variety of agents in a wide variety of bases. Though these preparations have shown high fungicidal activity in vitro they have rarely produced the expected clinical results, and it has been appreciated that many other factors are involved.

The two categories of infections which are most resistant to treatment are infections of the scalp due to the anthropophilic fungi and the group of infections due to *T. rubrum*. In both of these the host's reaction is minimal; and, until a method is devised of altering the host-parasite balance or of obtaining excretion through the skin of fungistatics or of substances which so modify the keratin that it becomes impermeable to fungal growth, treatment will have to be by topical application.

For some years we have made careful and detailed observations on both types of cases, and we feel that the problem is essentially the same in both groups—that of getting the fungicide or the fungistatic to the site where the fungus is growing. In scalp infections we have used salicylic acid, salicylanilide, phenyl mercuric nitrate, brilliant-green, and cuprammonium hydroxide in a wide variety of surface-active bases, including 'Carbowax,' 'Intraderm,' and different oil-in-water and water-in-oil emulsions. Carefully evulsed hairs from infected sites were examined microscopically, and the degree of penetration was assessed by appropriate counter-staining, but in no instance could we demonstrate to our satisfaction the presence of the reagent in the shaft of the hair below the upper limit of the internal root-sheath.

Much work has been done on the physical structure of hard keratin in the woollen industry, and it has been shown that the keratin molecules are so arranged that in the dry state they will only allow molecules smaller than propanol to pass between them. This structure can be opened up by saturation in water or by breaking intermolecular bridges by alkalis or other degrading agents, and larger molecules should then be able to penetrate. Similar modifications can be brought about in the soft keratin of the epidermis.

When keratin is degraded, however, fungi can attack it more easily in vitro (Barlow and Chattaway 1955); therefore clinical applications of such degrading agents should contain a fungicide freely soluble in water and preferably of small molecular size to increase the likelihood of its diffusing through the keratin.

Conversely, however, increasing the cross-linkages between keratin molecules diminishes attack by fungi, and we have felt it logical to attempt a combination of both methods.

Lithium bromide, which disrupts hydrogen bonds between keratin molecules, has already been used as a keratolytic (Rothman 1953), with considerable success when used continuously for several months. It takes a long time, however, and we felt that adequate penetration might be obtained by prolonged immersion in aqueous solutions of keratolytic agents.

Of the degrading agents which rupture hydrogen bonds we preferred urea to lithium bromide since it was considered less likely to cause epidermal reactions, and we used it in combination with sodium metabisulphite to break disulphide bridges as well. As a cross-linking agent between keratin molecules we chose ninhydrin (Cockburn et al. 1953) because it is easily detectable by the purple staining it produces, which indicates the depth of penetration achieved.

Keratin so modified has been shown to be less susceptible to attack by fungi in vitro (Barlow and Chattaway 1955). Five patients with resistant *T. rubrum* infections of the nails and corresponding soles were selected, and treatment was confined to one foot only. As a preliminary measure the nails were pared down, the greater part of the upper nail-plate was removed with a dental drill, and the foot was soaked continuously for six hours in the following solution:

| | |
|---|---|
| Sodium metabisulphite .. .. .. .. | 5 g. |
| Phenyl mercuric nitrate .. .. .. .. | 0·133 g. |
| Urea .. .. .. .. .. | 50 g. |
| Water to 100 ml. .. | |

With the addition of 0·1 % calsolene oil to 100 ml. of solution.

In one patient a slight reaction developed around the toes, and treatment had to be curtailed; but the other patients had no untoward symptoms. After six hours the soles and nails were kept continuously moist for two hours by spraying with a solution consisting of 2% ninhydrin and 0·133% phenyl mercuric nitrate in 50% ethanol. The whole treatment was repeated in forty-eight hours, and the feet were not washed for a week.

Scrapings taken five days after treatment showed that the outermost layers of the sole and nail and the fungus in them were freely stained by ninhydrin, but the deeper layers showed no staining and mycelium was present. Re-examination at the end of six weeks showed considerable improvement clinically, the nail-plates appearing normal and the soles less thickened. Scrapings, however, still contained mycelium although very much less than at the beginning of treatment and compared with the opposite (control) foot.

It is obvious that penetration was inadequate, possibly because urea is not so effective a keratolytic as lithium bromide. It must, however, be borne in mind that many of the fungicides in current use owe their activity to reactions with the protein of the fungus, and they probably react also with the proteins of the tissues. This is most certainly true of fungicides containing mercury, and this factor may make their penetration into the deeper layers of the epidermis more difficult.

The possibility of giving antimycotic drugs which are excreted as mercapturic acids in combination with keratin is attractive and seems to be a suitable line for inquiry (Spencer and Williams 1950), but unfortunately most of the substances that are excreted in keratin are toxic and unsuitable for clinical use. Patients who have had mepacrine for long periods, however, show altered fluorescence of hair and nails under Wood's light. Herrmann and Miller (1952) found this alteration in the hair-root, which fact suggests that mepacrine is excreted in combination with keratin. Although the alteration obviously does not affect the parasitism of the dermatophytes, we assessed the ability of fungi to attack such hair in vitro, and found that *M. canis* can invade such hair more freely than control hair.

### Conclusions

Our experiences with degrading and cross-linking agents underline the need for closer study of the barrier presented by keratin to the penetration of fungicidal agents into the deeper layers of the epidermis and into the lower two-thirds of the hair follicles.

Further progress in the treatment of persistent dermatophyte infections calls also for an increased knowledge of the metabolism of these organisms and of the many factors which determine their parasitism, including the effects of temperature, humidity, and their susceptibility to fungicides when growing parasitically.

We acknowledge a grant towards the cost of some of this work by the Agricultural Research Council. We thank Prof. J. B. Speakman for advice; Dr. Denton Guest for laboratory facilities; Mr. G. L. Mellor for pharmaceutical assistance; and Messrs. B. and L. Gosney for technical assistance.

### REFERENCES

Barlow, A. J. E., Chattaway, F. W. (1955) *J. invest. Derm.* **24**, 65.
— — Whewell, C. S. (1950) *Brit. J. Derm.* **62**, 251.
Cockburn, R., Jagger, L. G., Speakman, J. B. (1953) *Nature, Lond.* **172**, 75.
Gregory, P. H. (1935) *Biol. Rev.* **10**, 208.
Herrmann, F., Miller, O. B. (1952) *Acta derm.-venereol., Stockh.* **32**, 317.
Kligman, A. M. (1952) *J. invest. Derm.* **18**, 231.
— (1955) *Arch. Derm. Syph., Chicago*, **71**, 313.
Rothman, S. (1953) *Ibid*, **67**, 239.
Silva, M., Benham, R. W. (1954) *J. invest. Derm.* **22**, 285
Spencer, B., Williams, R. T. (1950) *Biochem. J.* **46**, 460.
Sulzberger, M. B., Baer, R. L. (1955) *Yearb. Derm. Syph.* p. 8.

# FRUCTOSE IN THE TREATMENT OF SEVERE DIABETIC KETOSIS

J. D. N. NABARRO
M.D. Lond., M.R.C.P.
ASSISTANT PHYSICIAN, MIDDLESEX HOSPITAL, LONDON

J. C. BECK *
M.D. McGill, F.R.C.P.(C.)
ASSISTANT PROFESSOR OF MEDICINE IN MCGILL UNIVERSITY, MONTREAL

J. M. STOWERS
M.A. Camb., M.D. Harvard, M.R.C.P.
LECTURER IN MEDICINE IN THE UNIVERSITY OF ST. ANDREWS

KETOSIS in diabetics is corrected by giving insulin, and in some cases glucose, to restore carbohydrate utilisation. There are good reasons for avoiding the use of glucose in the early stages of treatment of severe ketosis with a high blood-sugar level (Nabarro et al. 1952a). Briefly these are that, if the blood-sugar level is above 500 mg. per 100 ml., raising it further will not accelerate carbohydrate utilisation, although glycosuria and osmotic diuresis will be increased and rehydration delayed. Administration of glucose at this stage also makes it difficult to use changes of blood-sugar level as a guide to insulin requirements as treatment proceeds.

Reports from American centres advocate the use of fructose instead of glucose in the early stage of treatment of severe diabetic ketosis (Darragh et al. 1953, Dolger et al. 1953, Miller et al. 1953, Rosecan and Daughaday 1954). Duncan (1953) writes: "It is probable that the intravenous administration of fructose with the initial saline solution may well become part of our therapy for diabetic coma." Fructose has been used because it is removed from the blood as quickly in untreated diabetics as in healthy people (Weichselbaum and Daughaday 1951, Miller et al. 1952).

In diabetic ketosis it has been claimed that fructose given in the early stages does not aggravate the hyperglycæmia or osmotic diuresis (Dolger et al. 1953), that it increases carbohydrate utilisation (Miller et al. 1953), and that the plasma ketones disappear faster in patients treated with fructose and insulin than in those treated with insulin alone (Rosecan and Daughaday 1954).

It has also been suggested that giving a hypotonic sodium solution brought to isotonicity by the addition of 2·5% fructose allows of the administration of a proportion of "free water" to initiate cellular rehydration (Darragh et al. 1953).

With few exceptions the studies on which these claims have been based were made on cases of experimentally induced or mild ketosis. The investigations described here were made on patients admitted to hospital with diabetic ketosis. Preliminary observations were made of the effect of giving oral fructose without insulin to patients with moderate ketosis. Five patients with severe ketosis and high initial blood-sugar levels were given insulin and intravenous fluid to which fructose 50 g. per litre was added for the first 4–6 hours. The results were compared with those obtained in controls treated with insulin and a carbohydrate-free intravenous solution. In addition, two patients with severe diabetic ketosis but only slight hyperglycæmia were treated with insulin and intravenous fructose-containing solutions.

### Methods

In the cases of severe ketosis the initial dose of insulin was usually 100–200 units ($^1/_5$ intravenously and the remainder by deep intramuscular injection). Further doses were given at intervals of 2 or 3 hours, the amount depending on the blood-sugar level. The intravenous

* R. Samuel McLaughlin travelling fellow working in the Medical Unit, University College Hospital, from July to December, 1953.

fluid given in the initial stages was a saline-lactate solution (sodium 130 m.eq. per litre, chloride 100 m.eq. per litre, and lactate 30 m.eq. per litre). The first litre was given rapidly, and the patients received 2 or 3 litres in 4–6 hours. In the fructose-treated cases fructose 50 g. per litre was added. When the blood-sugar level had fallen appreciably, provided the excretion of urine was satisfactory, rehydration was continued with a glucose electrolyte solution containing glucose 50 g. per litre, sodium 20 m.eq. per litre, potassium 30 m.eq. per litre, magnesium 5 m.eq. per litre, phosphate 10 m.eq. per litre, and chloride 45 m.eq. per litre (Nabarro et al. 1952a).

On admission to hospital the patients were placed on a balance régime. Intake was by intravenous infusion, and all urine was collected, if necessary by an indwelling catheter. When possible, urine was obtained for a short period before treatment started. Specimens of blood, were taken frequently for estimation of sugar, ketones, urea, and electrolytes. The balance data have been corrected to a standard body-surface of 1·73 sq. metres to facilitate comparison of the fructose-treated and the control cases.

The chemical methods were those usually used in this laboratory (Nabarro et al. 1952b). Fructose was estimated

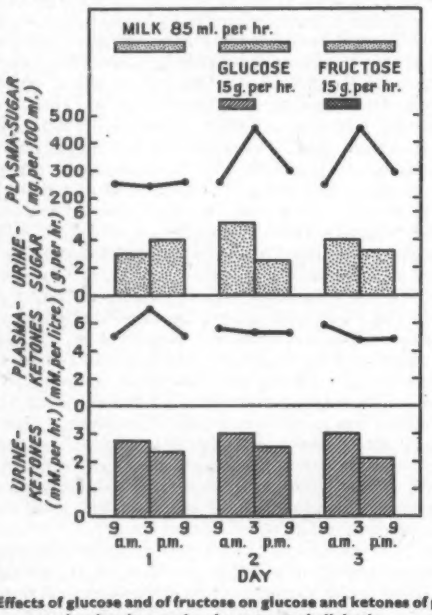



**Fig. 1—Effects of glucose and of fructose on glucose and ketones of plasma and urine in previously untreated diabetic.**

by the method of Higashi and Peters (1950) and plasma and urinary ketones by that of Greenberg and Lester (1944).

### Preliminary Studies

Three patients admitted with ketosis due to previously untreated diabetes were given fructose by mouth before they received any insulin. The first patient took 120 g. in 6 hours, and his plasma-ketone level, measured by the rough quantitative method of Dumm and Shipley (1946), fell from 12 mM. per litre to 8 mM. per litre. His blood-sugar level rose from 320 mg. per 100 ml. to 425 mg. per 100 ml., and his glycosuria increased from 2 g. to nearly 10 g. an hour. The plasma-fructose level and urinary excretion of fructose were negligible. From changes in the glucose level in the "glucose space" and in the urinary output of nitrogen and glucose it was estimated that less than half the fructose given was utilised or stored, the remainder being converted to glucose and for the most part excreted in the urine.

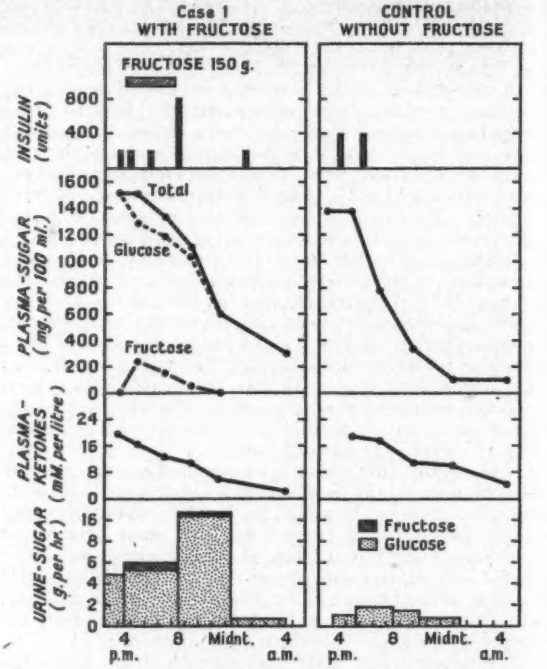



**Fig. 2—Results of treatment of case 1 with fructose and of control patient without fructose.**

The calculation was made as follows:

Fructose 120 g. was given in 6 hours. The plasma-glucose level rose from 384 mg. per 100 ml. to 500 mg. per 100 ml. The amount of glucose needed to do this, if the glucose space is assumed to be 30% of the body-weight, would be 22 g. Since 57 g. of glucose was excreted in the urine in the 6 hours, 79 g. of glucose became available during the period. 16 g. of this could be accounted for by gluconeogenesis (3·5 × urine nitrogen). From data obtained in a 4-hour control period before the fructose was given it appears unlikely that the remaining 63 g. of glucose came from any carbohydrate stores in the body. In the control period the glucose needed to raise the concentration in the body-fluids (3 g.) and the glucose in the urine (8 g.) almost exactly balanced the glucose derived from gluconeogenesis (10·6 g.). The unexplained 63 g. of glucose that became available in the fructose period was presumably from fructose; in addition 1 g. of fructose was excreted in the urine and 3 g. remained in the body-fluids. This leaves only 53 g. of the 120 g. originally administered for utilisation or storage.

TABLE I—5 CASES OF SEVERE DIABETIC KETOSIS TREATED WITH INTRAVENOUS FRUCTOSE

| Case no. | Sex | Age (yr.) | * | Blood-sugar (mg. per 100 ml.) | Plasma-bicarbonate (m.eq. per litre) | Plasma-ketones (mM. per litre) | Plasma-potassium (m.eq. per litre) | Fructose: Amount (g. per kg. of body-weight) | Fructose: Duration (hr.) | Insulin in first 12 hr. (units) |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | M | 71 | 1 | 1290 | 3·6 | 19·8 | 6·3 | 2·4 | 4·25 | 1600 |
| | | | 2 | 196 | 16·1 | 2·1 | 3·3 | | | |
| 2 | F | 69 | 1 | 725 | 5·0 | 16·0 | 5·7 | 3·7 | 4·25 | 950 |
| | | | 2 | 215 | 22·5 | 4·0 | 3·1 | | | |
| 3 | F | 36 | 1 | 600 | 5·0 | 16·0 | 6·7 | 2·3 | 6·5 | 920 |
| | | | 2 | 156 | 18·1 | 7·0 | 3·9 | | | |
| 4 | M | 28 | 1 | 530 | 1·3 | 28·5 | 4·9 | 1·9 | 5·5 | 500 |
| | | | 2 | 179 | 16·7 | 6·7 | 3·8 | | | |
| 5 | F | 26 | 1 | 388 | 4·0 | 13·3 | 5·4 | 1·4 | 4·25 | 280 |
| | | | 2 | 56 | 15·0 | 1·4 | 3·5 | | | |

*1, initial value; 2, 12-hour value.

The two other patients had mild ketosis (plasma-ketones 3–7 mM. per litre). They were given hourly milk feeds on 3 consecutive days; on the second day glucose 15 g. hourly was added to the milk for the first 6 hours, and on the third day fructose 15 g. hourly. The results in these two patients were similar (those obtained in one of them are shown in fig. 1). The effect on plasma and urinary ketones was slight, the most significant finding was that the rise of plasma-sugar level was as marked after fructose as after glucose. This sugar was all glucose, the plasma-fructose being negligible.

### Severe Diabetic Ketosis

Details of the five patients with severe ketosis treated with fructose are given in table I. Cases 1 and 2 were very ill on admission to hospital; each received 3 litres of the fructose-saline-lactate solution in just over 4 hours. The clinical improvement of all five patients was as rapid as that of patients treated without fructose. Plasma-

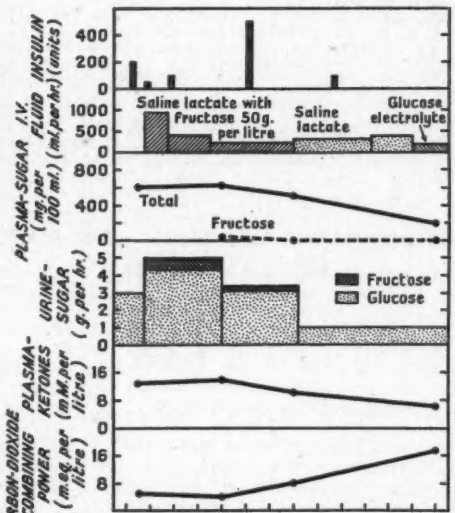



**Fig. 3—Slow fall of blood-sugar level in case 3 treated with fructose.**

ketone levels were estimated in only two of the controls; the rates of fall in case 1 and in a comparable patient treated without fructose are shown in fig. 2. The rise of plasma-bicarbonate level, which reflects to some extent the rate of fall of plasma-ketone level, is shown in table I. The improvement after 12 hours' treatment is similar to that obtained in the controls, in which the mean initial level was 5·0 m.eq. per litre, rising to 17·4 m.eq. per litre at 12 hours (the corresponding figures in the fructose-treated cases were 3·9 and 17·7). Ketonuria was abolished (negative Rothera test) by 6 hours in case 5, by 12 hours in cases 1 and 2, and by 18 hours in the two other fructose-treated patients, whereas in the controls it was abolished in 12–18 hours.

The mean initial blood-sugar levels and insulin requirements in the first 12 hours of the fructose-treated and control patients are given in table II. In addition to needing more insulin the patients receiving fructose tended to maintain their initial high blood-sugar level while the fructose was being given. This was not entirely due to fructose in the blood; the highest level found was 229 mg. per 100 ml. after the infusion of 100 g. in 90 minutes. The changes in blood-sugar level in case 1 and a comparable control patient are shown in fig. 2. The details of insulin dosage in case 1 indicate the difficulty of assessing insulin requirement while fructose is being given. Concern was also felt for case 3 because of the slow rate at which the blood-sugar level fell (fig. 3).

TABLE II—BLOOD-SUGAR, INSULIN DOSE, AND CARBOHYDRATE BALANCE FOR FIRST TWELVE HOURS

| — | No fructose (mean of 5 cases) | Fructose (mean of 5 cases) |
|---|---|---|
| Initial blood-sugar (mg. per 100 ml.) | 1048 | 707 |
| *Carbohydrate given (g.):* | | |
| Glucose | 59 | 56 |
| Fructose | .. | 145 |
| Insulin given (units) | 506 | 850 |
| Glycosuria (g.) | 24 | 45 |

The figures for carbohydrate intake and glycosuria have been corrected to a standard body-surface of 1·73 sq. metres.

Details of carbohydrate intake and excretion in the first 12 hours of treatment are also shown in table II. The fructose-treated patients retained a mean of 156 g. of carbohydrate out of 201 g. given, whereas the controls retained 35 g. out of 59 g. It is impossible to show whether the additional carbohydrate retained by the fructose-treated patients was utilised or stored. The reduction of plasma-potassium level (table I) was no greater than in the controls, and the excretion of potassium was slightly greater in the fructose-treated patients. If the extra carbohydrate retained were being stored as glycogen in the liver, an accentuation of the fall in the levels of plasma and urinary potassium would be expected.

The glycosuria in the controls was on an average 24 g. in the first 12 hours, and in the fructose-treated patients 45 g., made up of 41 g. of glucose and 4 g. of fructose. In view of the greatly increased carbohydrate intake of the fructose-treated patients the increase of glycosuria is small; this is presumably related to their higher insulin dosage.

The effect of the increased glycosuria on the urine volume and electrolyte excretion is shown in table III. Comparison of the two groups in this respect is not entirely satisfactory, because the fructose-treated patients received more fluid and extracellular electrolyte than did the controls. They lost a greater proportion of the infused fluid in the urine, but it seems unlikely that this was due to an osmotic diuretic effect.

### Discussion

If the early administration of fructose is to become part of the routine treatment of severe diabetic ketosis, it must be shown to improve the results and not to make the management of these cases more difficult. The chief benefit that has been claimed to follow the use of fructose is more rapid clearing of the ketosis. Rosecan and Daughaday (1954) compared the effect of insulin alone, insulin and fructose, and insulin and glucose on the rate of fall of the plasma-ketone level in experimentally induced episodes of mild ketosis. The fall was more rapid when insulin was given with glucose or fructose than when insulin and saline solution were given. In their study a fixed, rather small, dose of insulin was

TABLE III—WATER AND ELECTROLYTE BALANCE FOR FIRST TWELVE HOURS

| — | No fructose (mean of 5 cases) | Fructose (mean of 5 cases) |
|---|---|---|
| *Water (litres):* | | |
| Given | 4·6 | 5·0 |
| Retained | 3·4 | 3·4 |
| *Sodium (m.eq.):* | | |
| Given | 420 | 510 |
| Retained | 400 | 440 |
| *Chloride (m.eq.):* | | |
| Given | 350 | 410 |
| Retained | 310 | 350 |
| *Potassium (m.eq.):* | | |
| Given | 35 | 28 |
| Excreted | 26 | 51 |

Corrected to a standard body-surface of 1·73 sq. metres. No allowance has been made for either faecal or extrarenal losses.

given on each occasion ; the blood-sugar levels remained higher in the carbohydrate-treated episodes, and this may explain the increased rate at which the ketosis cleared. In the present five fructose-treated patients the ketosis cleared rapidly, possibly a little faster than in the controls and in other patients treated without fructose. It is difficult to be certain whether this is due to the fructose or to the larger insulin doses.

Rosecan and Daughaday (1954) found that the glycosuria was greatly increased by giving fructose but do not give figures for urine volume or electrolyte content. Miller et al. (1953), who made a similar study on one patient, reported that the urinary loss of water and electrolyte was not increased by giving fructose. Our present cases show that it is possible to avoid any great increase of glycosuria or osmotic diuresis when fructose is given to patients with severe diabetic ketosis, but that considerably more insulin is then required.

We had difficulty in some cases in judging the dose of insulin to be given. Published reports of the use of fructose in diabetic ketosis include only one where there was a very high blood-sugar level (Darragh et al. 1953, case 6b), and no reference has been made to this aspect of the problem. If the insulin dose is being assessed on alterations of the blood-sugar level, the administration of fructose gives rise to a further complication. The methods usually used for determining blood-sugar levels estimate both fructose and glucose. One of our patients with severe ketosis but only slight hyperglycæmia had an initial blood-sugar level of 260 mg. per 100 ml. She was treated with insulin and intravenous fructose and after four hours had a mild hypoglycæmic attack. The total blood-sugar level at the time was 130 mg. per 100 ml. Subsequently, when the blood-fructose level of the specimen was estimated, it was found that the blood-glucose was only 50 mg. per 100 ml., and fructose, which is not utilised by the brain, accounted for the remainder.

Solutions for the rehydration of patients with severe diabetic ketosis should be hypotonic as regards sodium (Butler 1950). If, however, the solutions given are too dilute, restoration of the extracellular fluids is likely to be delayed. The saline-lactate solution was suggested as a suitable fluid for rapid restoration of the extracellular fluid volume and at the same time allowing cellular rehydration to begin at an early stage (Nabarro et al. 1952a). Darragh et al. (1953) have studied the effect of giving a solution containing sodium 77 m.eq. per litre and fructose 2·5%. They showed that cellular rehydration started in the first 5 hours of treatment. In most of their cases there was no delay in the restoration of the extracellular fluid volume, but they had to give the infusions rather rapidly—4 litres in 3·6 hours in one case—and their patients had considerable glycosuria after treatment started.

### Summary

The effect of giving fructose to patients with diabetic ketosis was studied.

Oral fructose given without insulin to patients with mild ketosis lowered the plasma-ketone level. At the same time the blood-glucose level rose and glycosuria increased.

Five patients with severe diabetic ketosis were given insulin and intravenous fructose in the early stages of treatment. Their progress was compared with that of five patients treated without fructose.

Improvement in clinical condition was satisfactory in all the cases ; the ketosis possibly cleared a little quicker in the fructose-treated patients.

The administration of fructose tended to delay the fall of blood-sugar level and increased the insulin requirement.

Significant increase of glycosuria or of osmotic diuresis could be avoided if sufficient insulin was given, but it was more difficult to assess the amount needed.

There appears at present to be no reason for including the early administration of fructose in the routine treatment of severe diabetic ketosis.

These studies were initiated in the medical unit of University College Hospital Medical School, London, and continued (by J. D. N. N.) in the Institute of Clinical Research of the Middlesex Hospital, London. We thank Dr. F. V. Flynn and the staff of the biochemical laboratories of University College Hospital for some of the blood analyses, and British Drug Houses for the fructose. Many of the biochemical estimations were made by Miss Audrey Moxham. This work was supported by a grant from the Lund Research Fund of the British Diabetic Association. J. D. N. N. thanks the clinical research committee of the Middlesex Hospital for facilities and for a personal grant for research.

### REFERENCES

Butler, A. M. (1950) *New Engl. J. Med.* **243**, 648.
Darragh, J. H., Womersley, R. A., Meroney, W. H. (1953) *J. clin. Invest.* **32**, 1214.
Dolger, H., Kupfer, S., Bookman, J. J., Carr, J. (1953) *Ibid*, p. 562.
Dumm, R. M., Shipley, R. A. (1946) *J. Lab. clin. Med.* **31**, 1162.
Duncan, G. C. (1953) *Conn. St. med. J.* **17**, 493.
Greenberg, L. A., Lester, D. (1944) *J. biol. Chem.* **154**, 177.
Higashi, A., Peters, L. (1950) *J. Lab. clin. Med.* **35**, 475.
Miller, M., Drucker, W. R., Owens, J. E., Craig, J. W., Woodward, H. (1952) *J. clin. Invest.* **31**, 115.
— Murphy, J. R., Craig, J. W., Woodward, H. (1953) *J. clin. Endocrin.* **13**, 866.
Nabarro, J. D. N., Spencer, A. G., Stowers, J. M. (1952a) *Lancet*, i, 983.
— — — (1952b) *Quart. J. Med.* **21**, 225.
Rosecan, M., Daughaday, W. H. (1954) *J. clin. Invest.* **33**, 49.
Weichselbaum, T. E., Daughaday, W. H. (1951) *J. Lab. clin. Med.* **38**, 958.

## PERNICIOUS ANÆMIA IN THE SOUTH AFRICAN BANTU

J. D. WOODS
M.B. Witw'srand, F.R.F.P.S., M.R.C.P.

J. J. H. RYMER
M.A., M.B. Camb.

*From the Edendale Hospital, Pietermaritzburg, South Africa*

MEGALOBLASTIC anæmias associated with pregnancy or malnutrition are not uncommon in the Bantu races of Southern Africa (Foy et al. 1951, Adams and Wilmot 1953). Pernicious anæmia on the other hand is exceedingly rare. Trowell (1951) in Uganda first described a case, in a Ganda man. Adams and Wilmot (1953) in a paper on megaloblastic anæmias of pregnancy, said that they had seen one African woman in whom the clinical features were indistinguishable from those of pernicious anæmia. In neither of these patients were there any neurological symptoms. Foy et al. (1952) mentioned two cases of probable pernicious anæmia in East African women who had vague nervous symptoms. We record here a case in which prominent neurological features were made worse by folic acid and were relieved by vitamin $B_{12}$.

### Case-record

An African woman, aged 50, was admitted to this hospital in June, 1955, complaining of weakness of the legs. She stated that her symptoms had started about a month before admission. She was quite definite that she was of pure Bantu stock.

*On examination* the mucosæ were pale and the tongue smooth and red. There was no evidence of cardiovascular disease, except a soft systolic murmur. The legs were weak and the muscles slightly wasted. The knee-jerks were present, but the ankle-jerks absent ; no plantar response could be elicited. There was analgesia to the elbows and knees. Vibration and position senses were lost, the former up to the iliac crests. Romberg's sign was positive. The gait was grossly ataxic.

*Investigations.*—Blood-count : hæmoglobin 4·7 g. per 100 ml. ; packed-cell volume 14% ; mean corpuscular hæmoglobin concentration 33% ; white blood-cells 4800 per c.mm. (polymorphs 48%, lymphocytes 52%). A stained film showed anisocytosis, poikilocytosis, macrocytosis, and polychromasia. Radiographs of chest and spine normal. Cerebro-

spinal fluid, no abnormalities found. Fæces, no occult blood. Wassermann reaction negative in blood and cerebrospinal fluid. Gastric analysis, histamine-fast achlorhydria was found on two occasions. Bone-marrow megaloblastic.

*Treatment and progress.*—In view of the rarity in Africans of pernicious anæmia with subacute combined degeneration of the spinal cord, it was decided to treat the patient as a case of nutritional megaloblastic anæmia with polyneuritis associated with achlorhydria and to watch progress. Treatment consisted in administration of folic acid 20 mg. twice daily and vitamin-B complex ('Plebex') 2 ml. intramuscularly daily. The hæmatological response was good, and a maximum reticulocytosis of 36% developed by the eleventh day. At this time the hæmoglobin level had risen to 8·5 g. per 100 ml., and by the twenty-first day the level had reached 10·8 g. per 100 ml. Nevertheless the neurological condition deteriorated. The weakness of the legs increased and walking became almost impossible; and pain, which formerly had been absent, became prominent. The calf muscles became tender, but the reflexes remained unaltered.

The diagnosis was reconsidered, and vitamin $B_{12}$ in doses of 100 µg. daily was substituted for the folic acid. The hæmatological response was maintained, and after a further ten days the hæmoglobin level had risen to 12·9 g. per 100 ml. Two weeks after vitamin $B_{12}$ had been started the neurological symptoms had improved considerably. The pain had diminished and the patient could walk with less difficulty. The stocking-glove analgesia had been replaced by hyperæsthesia, but there was no indication of change in the lesions of the posterior columns of the spinal cord or in the tendon-jerks. The tongue was almost completely coated.

A *biopsy* specimen of the gastric mucosa, obtained at gastroscopy (Dr. P. Meyrick), was reported on as follows (Dr. G. Roach): "Sections show atrophy of the mucosa and a moderate plasma-cell infiltration. The glands are atrophic and show a marked metaplasia to a small intestinal type of gland. The histological picture is consistent with that associated with Addison's megaloblastic anæmia."

*Follow-up.*—The patient was then discharged from hospital and arrangements were made for treatment to be continued.

A month after discharge the patient reported back for re-assessment. She stated that she felt better and was walking with very little difficulty. The hæmoglobin level had reached 14·8 g. per 100 ml. There was a striking improvement in the neurological condition. All hyperæsthesia and analgesia had disappeared and vibration was felt as far down as the right ankle and the lower third of the left leg. Romberg's sign was absent, and the gait no longer ataxic. The reflexes were a little brisker and the plantar response was obtainable and was flexor.

### Discussion

The diagnosis of pernicious anæmia was established by finding megaloblastic anæmia, histamine-fast achlorhydria, and a characteristic gastric mucosa. This diagnosis was further supported by the response to treatment of the neurological disorder. It is well known that folic acid aggravates subacute combined degeneration of the spinal cord associated with pernicious anæmia, and that this is relieved by vitamin $B_{12}$ in large doses. This feature was well illustrated here. The patient apparently had early subacute combined degeneration of the spinal cord without severe involvement of the pyramidal tracts.

### Summary

A case of pernicious anæmia and subacute combined degeneration of the spinal cord in a pure-bred South African Bantu woman is described.

The patient's neurological disorder deteriorated during treatment with folic acid but greatly improved when instead vitamin $B_{12}$ was administered.

We thank the director of the Natal Provincial Medical Services and Dr. J. Parker, medical superintendent of Edendale Hospital, for permission to publish this case; and Dr. W. Laurie, Dr. K. C. Watson, Dr. M. Addison, and Dr. G. Roach, of the Natal Pathology Service, for their help.

### REFERENCES

Adams, E., Wilmot, A. *S. Afr. med. J.* (1953) **27**, 1028.
Foy, H., Kondi, A., Hargreaves, A. (1951) *Lancet*, i, 380.
— — — (1952) *Trans. R. Soc. trop. Med. Hyg.* **46**, 327.
Trowell, H. (1951) *Lancet*, ii, 761.

# ECZEMA VACCINATUM
## WITH VACCINIAL LESIONS STRICTLY CONFINED TO THE ECZEMATOUS PATCHES

LUIS F. DE SALLES-GOMES
M.D.
*From the Virus Section, Instituto Adolfo Lutz, São Paulo, Brazil*

ORLANDO NATALE BASSOI
M.D.
*From the Department of Tropical and Infectious Diseases, School of Medicine, University of São Paulo*

LUIS DIAS PATRICIO
M.D.
*From the First Medical Clinic, Hospital das Clinicas, University of São Paulo*

ECZEMA vaccinatum has long been known under the names of pustulosis acuta varioliformis, pustulosis acuta vacciniformis, postvaccinal eruption, eczema varicellatum, Kaposi's varicelliform eruption, and generalised vaccinia. Ronchese (1943) suggested the name dermatitis vaccinica, but it seems better to use "eczema vaccinatum" for a vaccinial eruption associated with eczema and "eczema herpeticum" for herpetic lesions associated with eczema; the clinical picture of these two associations may be identical. There is still another association of eczema with a vesicular rash from which no virus has been isolated (van Rooyen and Rhodes 1948a).

In the previously published cases of eczema vaccinatum the vaccinial pustules appeared not only in the eczematous patches but also surrounding them; in some cases there was true generalised vaccinia. In the case described here the vaccinial lesions were strictly localised. The diagnosis was established by isolation and identification of the vaccinia virus from the pustules and by the clinical history.

### Case-report

A white boy, aged 2 years, was admitted on Sept. 23, 1954, with the clinical diagnosis of eczema vaccinatum. Five days earlier his mother had noticed that eczematous patches which he had had at the back of his knees for one and a half years had become swollen, hot, and painful, and he had a temperature of 104°F, and was restless and anorexic. Two days later purulent vesicles, 5–6 mm. in diameter, appeared in both popliteal regions. Since then his temperature had been 98·6–104·0°F. In the next two days the vesicles increased in number but not in size and were exclusively restricted to the patches of eczema, which were pruriginous and painful. On the first day of the present illness the child had had a sore throat and a very painful enlarged right crural lymph-gland. Two days later a left crural lymph-gland became enlarged.

*Previous History.*—For three months from birth the patient had eczema of the scalp; when this disappeared, his neck became eczematous. The eczema disappeared later from the neck, and for the last one and a half years only two eczematous patches had been present, one in each popliteal region. The patient had never been vaccinated, but his mother had been vaccinated against smallpox twenty days before his admission, and he had been scraping one of her vaccination pustules.

*On examination* he was in good physical condition, with temperature 102·2°F, pulse-rate 160, respirations 52 a minute, and blood-pressure 100/60 mm. Hg. A hard painful lymph-gland about the size of a pigeon's egg was palpable in each crural region. The pharynx, tonsils, and tongue were hyperæmic. In each popliteal region was a well-demarcated infiltrated eczematous patch with numerous confluent umbilicated greenish-yellow pustules (see figure). An erythematous halo surrounded both patches.

*Investigations.*—Biopsy of a lesion showed degenerated cells, numerous lymphocytes, and few epithelial-cells. Bacteriological examination of the contents of the pustules showed streptococci and micrococci. The search for a virus is described below.

Popliteal patches of eczema vaccinatum.

*Treatment and Course.*—Gauze impregnated with yellow soft paraffin and nitrofurazone was used as a local dressing and vitamins A, D, and B-complex were given. For four days after admission the boy's temperature was 98·6–99·7°F; later it became normal. Two days after admission the pustules in the right popliteal region burst, except some which were crusted and later shed their crusts, exposing an easily bleeding surface. The pustules in the left popliteal region dried up and developed crusts. The crural lymph-glands became smaller and less painful. Six days after admission a purulent exudate appeared on both eczematous patches and quickly responded to treatment. Recovery began on the thirteenth day after the onset of the rash. Eight days later the boy was discharged with only the eczematous patches visible.

### Search for Virus

One sample was collected from each eczematous patch. Each sample consisted of the roof of several pustules because no fluid was then present in the pustules. Both samples were ground separately and suspended in 0·5 ml. of broth. Penicillin and streptomycin were added to these inocula and allowed to act for 30 minutes at room-temperature. The chorio-allantois of 10-day hen s eggs was inoculated by the standard Burnet technique. Eggs opened after 3 days' incubation at 37°C showed heavy bacterial contamination. The original inocula were then treated with chloramphenicol (Hall et al. 1953), after which inoculation yielded typical vaccinia-virus lesions on the chorio-allantois. Four serial passages were then made, every one of which yielded the same appearance, which fact has considerable diagnostic value (Downie and Dumbell 1947, MacCallum 1954).

One of the chorio-allantoic membranes from the fourth passage was suspended in broth at $10^{-1}$ concentration for use as inoculum in inoculation of rabbit skin and cornea. After the skin had been shaved, the inoculum was spread on the skin of one side and on the cornea on the same side. Scarifications were then made at both places with a sharp scalpel. The cornea exhibited a slight opacity on the second day after inoculation, and severe keratoconjunctivitis on the third day. Scrapings of the cornea were inoculated on the chick-embryo chorio-allantois after treatment with penicillin and streptomycin. Typical vaccinia-virus lesions developed. Inoculation of rabbit skin yielded confluent papular lesions which strictly followed the scarification tracts; these had purposely been made well apart. On the fourth day vesicles were apparent, and on the sixth day recovery began. A biopsy specimen of a vesicle on the fourth day was fixed in Helly's fluid and showed the typical histology of vaccinial lesions in rabbit skin (Amies 1938). Only intracytoplasmic inclusion bodies were observed.

An anti-vaccinia hyperimmune rabbit showed no lesion on the skin and cornea after inoculation by scarification with the virus isolated from the patient's right leg. The activity of this challenge was tested by simultaneous inoculation on the chick-embryo chorio-allantois, and typical vaccinial lesions were again observed. The rabbit had been hyperimmunised by several inoculations of the vaccinial calf-lymph used at the Butantan Institute of São Paulo for preparing anti-smallpox vaccine. This strain has received numerous calf-skin passages for a long time, with yearly passages on rabbit skin, and it has been used in millions of human vaccinations. The first inoculation for hyperimmunisation was made on the rabbit skin and cornea. Typical reactions were seen at both places. Three subcutaneous inoculations were later made at weekly or slightly longer intervals; 0·5 ml. of $10^{-1}$ broth dilution of the lymph being injected in each subcutaneous inoculation.

A neutralisation test (Scott et al. 1949) was made on the chorio-allantois. A pool of sera from two rabbits, hyperimmunised with the Butantan Institute vaccine lymph as has just been described, was used as well as the virus isolated from the patient. From $10^{-1}$ to $10^{-6}$ dilutions of chorio-allantoic membranes inoculated with the latter virus were mixed with an equal volume of hyperimmune serum diluted 1 to 16 in saline solution. The mixture was then incubated in the ice-box for one and a half hours. Inoculation on the chorio-allantois of 10-day eggs was made with 0·05 ml. of this mixture per egg. There was neutralisation in the mixtures containing $10^{-3}$ and $10^{-4}$ dilutions of the virus, which showed a significant decrease in the number of lesions compared with the controls. The latter were inoculated with the same virus dilutions mixed with an equal volume of a 1 to 16 dilution of normal rabbit serum.

### Discussion

The data given above leave no doubt about the diagnosis. Eczema typical in localisation, morphology, recurrency, and therapeutic response existed before the accidental infection with vaccinia virus. One of us (L. D. P.) had treated the child for several months before. Contact with the recently vaccinated mother was very suggestive. The appearance of pustules and their localisation also indicated eczema vaccinatum. The identity of the vesiculopustular rash was established through isolation and identification of vaccinia virus from several of these lesions. Various tests of pathogenicity, pathology, serology, and immunology satisfactorily identified the agent isolated from the pustules as vaccinia virus. The vaccinia-virus strain used as standard in the serologic and immunologic tests was the one used in vaccinating the patient's mother, who apparently was the source of contagion. Accidental contagion of vaccinia in a family has been reported by Gray (1948).

The appearance of lesions on the chorio-allantois, which has considerable diagnostic value (Downie and Dumbell 1947, MacCallum 1954), the behaviour on rabbit skin and cornea, and the results of neutralisation and immunologic tests completely eliminate herpes-simplex virus as the causal agent of the vesiculopustular rash. The behaviour of the isolated agent on the chick-embryo chorio-allantois and rabbit skin and cornea also eliminates variola virus. The neutralisation and immunologic tests are of little or no value in differentiation with variola virus owing to known group cross-reactions (McCarthy and Downie 1948).

As regards the method of contagion, since the child used to scrape his mother's vaccine pustule, direct inoculation on to his pruriginous eczematous lesions seems at first obvious, but analysis of the clinical data does not

support this hypothesis. Lesions appeared simultaneously on both eczematous patches and immediately spread. If the portal of entry was the eczematous lesions, one would expect only a few lesions to appear on one leg only, on the same side as the hand which the child used to scrape his mother's vaccine pustule. Scratching on the popliteal region of the opposite side seems to be difficult, and would provoke lesions localised in a suggestive manner: the primary lesions, or lesions of inoculation, would appear just along the scratching paths in the same way that lesions appear on the scarification lines from inoculated rabbit skin. Finally, the secondary lesions would have appeared after an interval, as in generalised vaccinia. The rapid spread of the lesions and the identical developmental stage of the pustules seen on examination of the patient indicate that all the lesions originated from the same rash.

The strict limitation of vaccinial lesions to the eczematous patches as well as the data presented above can, in all probability, be interpreted as a result of hæmatogenous spread of the vaccinial infection. The agent probably entered the body through the respiratory tract and not through the eczematous lesions. In all probability it provoked external (skin) lesions in the locus minoris resistentiæ (the eczematous patches) during a viræmic phase of infection. Abundant clinical and experimental data clearly indicate a relationship between the appearance of vaccinia lesions on the skin of numerous hosts and the pre-existence of allergic lesions or various generalised conditions of the skin (van Rooyen and Rhodes 1948b). We have not been able to find any published report of such strict localisation as was found in the present case, but a similar example was reported of eczema herpeticum (Leider 1951).

Ohtawara (1922) was the first to call attention to the hæmatogenous origin of generalised vaccinia skin lesions, and numerous experimental and clinical reports have confirmed his findings. Special attention should be called to Fenner's (1948) thorough study of the pathogenesis of skin lesions in ectromelia, another member of the variola-vaccinia group. The demonstration by Downie et al. (1950) of a viræmic phase in human variola is also worthy of mention.

**Summary**

In an eczematous child who used to scrape his mother's vaccine pustule vaccinial lesions appeared which were strictly confined to the eczematous patches on both popliteal regions.

The vaccinia virus was isolated and identified.

The probability of a hæmatogenous origin of the vaccinial lesions is discussed.

We are indebted to Dr. Juan J. Angulo, of the Instituto Adolfo Lutz, for advice and criticism about the laboratory work and for help in preparing this paper.

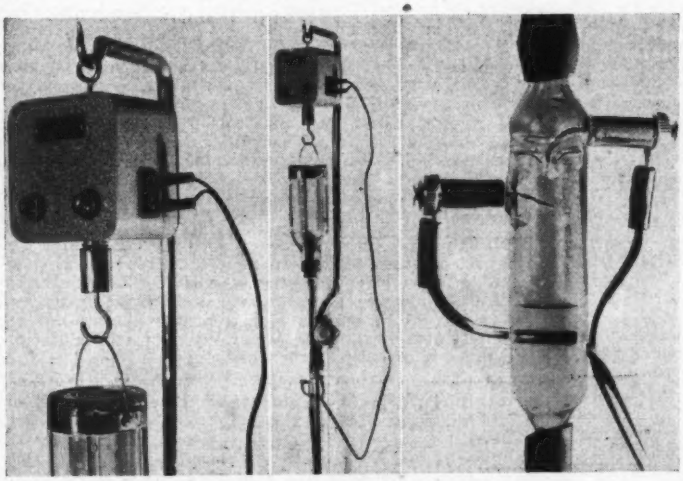
REFERENCES

Amies, C. R. (1938) *J. Path. Bact.* **47**, 205.
Downie, A. W., Dumbell, K. R. (1947) *Ibid.* **59**, 189.
— McCarthy, K., Macdonald, A. (1950) *Lancet*, **ii**, 513.
Fenner, F. (1948) *Ibid*, **ii**, 915.
Gray, F. G. (1948) *Bull. Johns Hopk. Hosp.* **82**, 538.
Hall, G. F. M., Cunliffe, A. C., Dudgeon, J. A. (1953) *J. Path. Bact.* **66**, 25.
Leider, M. (1951) *Arch. Derm. Syph., Chicago*, **63**, 456.
MacCallum, F. O. (1954) *In* The Dynamics of Virus and Rickettsial Infections. New York; p. 330.
McCarthy, K., Downie, A. W. (1948) *Brit. J. exp. Path.* **29**, 501.
Ohtawara, T. (1922) *Sci. Rep. Inst. infect. Dis. Tokyo Univ.* **1**, 203.
Ronchese, F. (1943) *Arch. Derm. Syph., Chicago*, **47**, 613.
Scott, T. F. M., Coriell, L. L., Blank, H. (1949) Diagnosis of Viral and Rickettsial Infections. New York; p. 88.
van Rooyen, C. E., Rhodes, A. J. (1948a) Virus Diseases of Man. New York; p. 299.
— — (1948b) *Ibid*, p. 391.

# New Inventions

## THE BARTS-ENFIELD DRIP INDICATOR

IN these days of automation, when our understaffed hospitals are still so wary of mechanical and electrical aids to nursing that methods discarded by industry fifty years ago are still normal practice, we welcomed the Matburn electrical drip-recorder, described by Evans,[1]



as a first step towards the introduction of labour-saving devices into the wards.

The recorder enables a night-nurse in a darkened ward to observe the rate of a transfusion at a glance and from anywhere in the ward without interrupting her other duties. However, it falls short of providing complete control by failing, until too late, to give any indication of when a bottle is running out.

A companion device has therefore been designed to provide this information. Essentially it is a specially sensitive spring-loaded switch, which illuminates a steady warning light when the weight of the bottle and its contents falls to a predetermined level. Experimental weighings of numerous standard pint transfusion bottles containing the usual intravenous solutions showed that the variation in weight was small enough, when a small quantity remained in the bottle, to allow the device to be reasonably accurately preset. It can, however, be adjusted for alterations in weight.

At a later stage it was decided, with permission from Dr. Frankis Evans, to incorporate the two devices in one comprehensive drip-control unit, to be known as the Barts-Enfield drip indicator. The warning device can be used alone if required, and it is set in action simply by hanging it from a support and suspending the bottle from the hook underneath.

The unit is powdered by one high-tension battery and uses neon bulbs, so that the current drain is very small and the battery should be almost everlasting. The device can be adapted for use with a buzzer, but the visual warning is usually adequate and far less disturbing.

The unit was produced by Mr. J. T. Burns, of Messrs. Matburn Ltd., to whom I am indebted for his invaluable assistance in translating a crude prototype into the virtually foolproof finished product. I must also thank Mr. Hardwicke Knight for his excellent photographs.

Since preparing this note for publication I have learnt that a drip alarm on similar principles, though mechanically somewhat different, has already been described.[2]

Chase Farm Hospital,
The Ridgeway,
Enfield, Middlesex

DAVID ZUCK
M.B. Birm., F.F.A. R.C.S., D.A.

1. Evans, F. T. *Lancet*, 1955, i, 29.

2. Bottoms, R. W. A. *Ibid*, 1954, i, 1167.

# Reviews of Books

## Studies in Tuberculosis

R. G. FERGUSON, M.B.E., B.A., M.D., LL.D., former director of medical services and general superintendent, Saskatchewan Anti-Tuberculosis League. Toronto: University of Toronto Press. London: Oxford University Press. 1955. Pp. 124. 28*s*.

IN the prairie districts of Canada the decline in tuberculosis mortality came sooner than elsewhere, and this book epitomises the considerable experience and careful epidemiological observations of the staff of the Saskatchewan Anti-Tuberculosis League.

The author's views, clearly the result of logical thinking on much data, are carefully expressed, with words used so sparingly that sometimes the reader must concentrate very hard. One of the hazards of the epidemiological approach is the tendency to concentrate mainly on the infective and hereditary aspects; and here this is not altogether avoided. Comparatively little account is taken of stress factors which lead to breakdown in those whose first infection has healed.

The rôle of infection, however, is submitted to such a searching examination that modern thought on the subject is advanced a stage or two further, particularly in relation to the part played by the "summation" of all infections; and the effect of infection on the already infected also receives much-needed scrutiny. The importance of inherited resistance is accorded due recognition and the natural course of a tuberculosis epidemic is rationally analysed. Finally, the foundations of a preventive programme are presented and Dr. Ferguson attempts to answer some of the more difficult questions about the length of follow-up required for patients and their contacts.

This valuable book illustrates a type of thinking along epidemiological and preventive lines to which many people in this country are now beginning to turn.

## Allergy and Anaphylaxis

KEIZO NAKAMURA, M.D., professor of bacteriology, Nippon Medical School, Tokyo. Tokyo: Nippon Medical School. 1955. Pp. 114.

FROM the results of orthodox animal experiments, mainly with diphtheria toxin, Professor Nakamura concludes that antitoxic immunity and toxin anaphylaxis are due to the same antigen-antibody reaction, the former involving blood-borne antibody, the latter antibody in tissue. Anaphylaxis and allergy have the same basic mechanism.

Evidence is brought forward that acetycholine is released in anaphylactic reactions, the effects of which are potentiated by organic phosphorus drugs with anticholinesterase activity. Synthetic anti-histamine drugs with appreciable anti-acetylcholine activity reduce the symptoms of anaphylaxis, while those with weak anti-acetylcholine action are less effective, even if their anti-histamine activity is potent. The author therefore stresses the rôle of acetylcholine, and hence the autonomic nervous system, in the mechanism of allergy and anaphylaxis.

This readable book is also of value because it summarises Japanese work on this subject over the past twenty years, and much of this has not previously been recorded in a European language.

## Psychocutaneous Medicine

MAXIMILIAN E. OBERMAYER, M.D., clinical professor and chairman, department of dermatology, School of Medicine, University of Southern California. Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1955. Pp. 487. 70*s*.

THE most comprehensive work yet published on the significance of emotional factors in dermatology, this book tackles a subject which still causes a good deal of argument; and more heat will no doubt be raised by the choice of "psychocutaneous" for the title. "Psychodermal" would have been more satisfying to the purist, but "dermatological neuroses," as used by O'Donovan, has probably not been bettered.

After a brief historical review, there is a very useful chapter by Dr. Richard D. Evans on dynamic considerations of the psyche. This should help to make the rest of the book more intelligible to those readers who are not familiar with the technical language and modern concepts of psychological mechanisms. The chapter on theories of mechanisms and methods of study should be read by anyone contemplating research in dermatological neuroses. The author then deals with the true dermatoneuroses and dermatoses in which emotional factors are in varying degrees significant. Finally, he discusses the diagnostic approach and the rôles of the dermatologist and the psychiatrist.

There are over 100 clinical photographs, presumably intended to help readers unfamiliar with skin diseases; but, even so, it seems excessive to show, for example, 8 pictures of neurodermatitis, including 3 of lichenification of the antecubital regions. It is stretching the psychogenic theme to its limit to include molluscum contagiosum, and surprising to see 5 pages (and 3 clinical photographs) on emotional factors in lupus erythematosus.

Readable, stylishly written, and well produced, this book is a reasoned and (as far as can be) unbiased yet critical review: all opinions receive their fair share of attention.

## Moderne Therapie der Anämien

WALTER TISCHENDORF, professor at the University of Göttingen. Stuttgart: S. Hirzel. 1955. Pp. 115. DM. 14.

TREATMENT is classified by Professor Tischendorf according to the pathogenesis of the anæmia—hæmolytic, deficiency, or myelopathic. The theoretical background for certain types of treatment is well discussed; there is, for instance, a complicated diagram showing the relationship between folic acid, vitamin $B_{12}$, and other substances active in megaloblastic anæmias. On the whole the treatment recommended follows standard Anglo-American practice, but it is surprising to see that folic acid is advised for pernicious anæmia. The doses recommended for vitamin $B_{12}$ are much smaller than are now given in this country.

## L'hérédité en médecine

*Caractères, maladies, correlations.* A. TOURAINE, membre de l'Académie de Médecine. Paris: Masson. 1955. Pp. 875. Fr. 7200.

Dr. Touraine is a French physician with a special interest in genetics. He has written this book for his French colleagues to interest them in medical genetics and also to serve them as a work of reference.

There are two sections: the first deals with general principles and the second covers systematically the genetics of each bodily system. The book, therefore, is a French equivalent of the recent English publication *Clinical Genetics*, edited by Professor Sorsby; but it is the work of a single author. The clinical section is remarkably comprehensive but does not attempt to be critical. The approach is through the inspection of individual family trees rather than through analysis of the frequency with which different degrees of relatives are affected. The genetics of physiological as well as pathological characters are discussed. The section on dermatology is especially good. For English readers the book will also be useful as a source of reference to Continental publications.

Dr. Touraine also includes a sensible chapter on the social application of human genetics. He sees positive eugenics in terms of social measures to raise the birth-rate, by improving the standard of living, of classes of society where favourable hereditary characters are especially common. Quantity and quality of population, he considers, are objectives to be pursued together.

---

**Administrative Medicine** (New York: Josiah Macy, jun., Foundation. 1955. Pp. 172. $3).—The transactions of the third conference on this subject, sponsored by the Foundation, which was held at Princeton in October, 1954, have now been published under the editorship of Dr. George S. Stevenson. The scope of the discussion is indicated by the attributes and talents which members of the conference thought necessary for the ideal administrator. A list of 14 supplied by Dr. A. J. J. Rourke included the humanitarian talents of a physician, the system and order of an accountant, the equilibrium of a philosopher, the flexibility and agility of a fox, the blending abilities of a baker, and a crystal ball to look into the future.

THE LANCET
*LONDON: SATURDAY, DEC. 17, 1955*

## Poliomyelitis in 1955

THE story of poliomyelitis vaccines has shown a remarkable series of changes in the year now ending, and 1955 will probably be regarded in the future as a landmark in the history of the disease. A dramatic account of the year's happenings in the United States was given last week by Dr. ALEXANDER D. LANGMUIR, of the Communicable Disease Center, U.S. Public Health Service, Atlanta, to a meeting of the section of epidemiology of the Royal Society of Medicine. The favourable results announced on April 12 of the big field trial of the Salk vaccine encouraged the U.S. Public Health Service to authorise the production and release of vaccine by six commercial firms. In an extraordinarily short time a huge vaccination programme was under way, but within two or three weeks there followed what Dr. LANGMUIR described as an epidemiological disaster. A number of cases of paralytic poliomyelitis were associated with inoculation of vaccine prepared by the Cutter Laboratories; and the circumstances left no doubt that this was a common-source epidemic for which the vaccine was directly responsible. Altogether 204 cases, including 11 deaths, were accepted by the poliomyelitis surveillance unit as associated with Cutter vaccine. Of these cases, 79 were in vaccinated persons, 105 were in family contacts of vaccinated persons, and 20 were in community contacts. It seems remarkable that so few community contacts were involved; after the first few infections had appeared the numbers of cases among vaccinated persons and family contacts behaved much as expected, but Dr. LANGMUIR disclosed that the numbers among community contacts were very much smaller than was at one time feared. Laboratory investigation later confirmed what was very soon clear from epidemiological evidence—namely, that live poliomyelitis virus (type 1) was present in certain batches of the Cutter vaccine. There were two further incidents: a few cases were reported from Pennsylvania and Maryland among children inoculated with vaccine prepared in the Wyeth laboratories and also among family and community contacts of these children. Particularly in Maryland, the circumstances raised strong suspicion that this was not fortuitous, but after extensive laboratory tests no poliomyelitis viruses were isolated from the vaccine. A detailed study of the methods of preparing and testing the safety of the vaccine was at once undertaken by the U.S. Public Health Service, and, as a result, stricter safety standards for the manufacture and testing of vaccine were imposed. Since then constant epidemiological surveillance has revealed no further evidence of a significant association between poliomyelitis and any lot of vaccine.

The second task of the poliomyelitis surveillance programme described by Dr. LANGMUIR was to evaluate the efficacy of vaccination carried out in 1955. This was not a strictly controlled study, and there were stops and starts in the vaccination programme during the Cutter incident; it is therefore extremely hard to assess accurately the value of the vaccine. The surveillance unit made an elaborate investigation of the incidence of poliomyelitis in vaccinated children and compared the figures with those in unvaccinated children. So far not much stress has been laid on the number of doses of vaccine given and many of the children received only a single dose. Among preliminary reports from a number of States, figures for New York give paralysis rates of 4·0 per 100,000 for vaccinated children and 20·9 per 100,000 for unvaccinated children. Similar figures for Minnesota, where the difference between the two groups is largest, are 2·7 for the vaccinated and 30·1 for unvaccinated children. In Georgia, where the difference is smallest, the paralysis-rate for vaccinated children is 3·4 per 100,000, compared with 7·6 per 100,000 unvaccinated. There were usually smaller differences when the rates of non-paralytic poliomyelitis were compared in the two groups, but here confusion is likely from the inclusion of cases of aseptic meningitis, as Dr. J. H. S. GEAR emphasised in the discussion at the Royal Society of Medicine. So far as can be judged at present, these results show the same order of efficacy as was found in the 1954 vaccine trial. But Dr. LANGMUIR was well aware of the possibilities of error in arriving at these figures, and he looked for independent confirmation of the findings. A study of the age-distribution of paralytic poliomyelitis showed that in children aged 7 and 8 the attack-rate was lower than in younger and older children. Since poliomyelitis vaccine was most widely used in children of 7 and 8 this finding, which is in contrast to the experience of other years, is taken as independent evidence that the vaccine protects against paralytic poliomyelitis. This method does not, of course, give a quantitative estimate of the effectiveness of the vaccine.

The World Health Organisation recently held a study-group in Stockholm on poliomyelitis vaccine.[1] Experts from eight different countries reported their experience with the use of inactivated vaccines, and apart from the incidents in the U.S.A. no paralytic poliomyelitis developed in circumstances which suggested that the vaccine was to blame. The Salk vaccine, it was concluded, offered good protection to children aged 6–10—the only age-group for which sufficient evidence had been gathered to justify a conclusion. In Canada, preliminary results showed an attack-rate of paralytic poliomyelitis of 1·07 per 100,000 for vaccinated children and 5·39 per 100,000 among unvaccinated children. In Denmark, there were no cases of paralytic poliomyelitis among over 400,000 vaccinated children, but only 7 cases of paralytic poliomyelitis were reported in the whole of Denmark this summer. In this country, vaccine was made but was never issued for use, because of the doubts about its safety; the vaccine now in commercial preparation is being made with a less virulent type-1 virus than that hitherto used in the U.S.A.

Hopefulness about poliomyelitis vaccines is slowly returning, and the outlook, as the year ends, is brighter than seemed even remotely possible a few months ago. Many people feared that the Salk vaccine had been used for mass inoculation before its safety was

1. See *Lancet*, Dec. 3, 1955, p. 1199.

assured, and that the understandable enthusiasm of those who were convinced of the vaccine's value had carried them close to catastrophe. Nothing that has happened since has convinced us that these fears were unfounded, but there is now no doubt that the 1955 programme of poliomyelitis vaccination in the United States was a bold step towards the conquest of the disease. The more venturesome policy has been at least partly justified by information quickly gained about the vaccine's powers. With the new safety tests, the Stockholm meeting felt that the chances of producing paralytic disease by vaccination were extremely small. But at least one important question cannot yet be answered: is vaccine which has satisfied the new safety standards undiminished in its protective power? And there are several other unknowns, particularly concerning the duration of protection. Moreover, there are many possibilities of improvement towards a better vaccine, and the W.H.O. group are anxious to encourage further research with live attenuated virus.

## Dermatomyositis

RAREST of the collagen diseases, dermatomyositis can present a difficult exercise in diagnosis. A study of what has been written about this disease is apt to leave the reader with a confusing picture of widely varying clinical patterns; and DOMZALSKI and MORGAN, in a recent review,[1] have done well to emphasise the central theme of non-suppurative polymyositis with dermatitis and œdema, the triad on which a secure diagnosis must finally be based. A bewildering variety of skin eruptions have been described—erythematous, erysipeloid, macular, papular, telangiectatic, purpuric, vesicular, bullous, ulcerative, exfoliative, or psoriatic. The skin may be shiny or dull, thickened or atrophic, scaly or wrinkled like parchment. Hypertrichosis, alopecia, hyperhidrosis, photosensitivity, and Raynaud's phenomenon may occur. Follicular keratosis, pitting of the finger-nails, dermographia, urticaria, erythema nodosum, and erythema multiforme have all been described—as, on the other hand, has a complete absence of changes in the skin. From this array the most characteristic manifestation is probably cutaneous telangiectasia, associated with periorbital œdema and discoloration—KEIL's "heliotrope eyelids."[2] The signs of myositis are more constant and the diagnosis cannot be seriously countenanced in their absence. Pain, weakness, and stiffness are the cardinal symptoms, and the neck, shoulder, and pelvic girdle their commonest sites. Weak muscles may on occasion feel normal, though more often they are tender, swollen, and doughy at first, and hard and fibrotic later. Contractures are common, and if the muscles of respiration and deglutition are involved the patient may die of asphyxia or of aspiration pneumonia.

The only really helpful laboratory aid is the measurement of creatine in the urine. Normal adult men excrete little or no creatine, but women, children, and elderly men excrete up to 400 mg. in twenty-four hours. In dermatomyositis creatine is excreted in large amounts—up to 1100 mg. in twenty-four hours.[3] Unfortunately creatinuria is encountered at times in other conditions,[4 5] including systemic lupus erythematosus, which may be difficult to distinguish from dermatomyositis; demonstration of the lupus-erythematosus-cell phenomenon is helpful. A biopsy of muscle is sometimes of value, but the histological changes of dermatomyositis are not specific and may not be found in a small sample of tissue. Dermatomyositis shares with scleroderma a distribution of lesions in skin, muscles, and heart. Calcinosis is common in both, but involvement of the pulmonary and alimentary systems is a feature only of scleroderma, and the early skin changes of dermatomyositis tend later to recede. Differentiation of dermatomyositis from rheumatoid arthritis is usually easy: stiffness and contractures are common to both, but actual arthritis is rare in dermatomyositis. Exceptionally, changes indistinguishable from rheumatoid arthritis have been described.[6 7] Of 9 patients reported on by JAGER and GROSSMAN,[8] 3 had arthralgia without swelling of joints; and O'LEARY and WAISMAN[3] found arthritis in 2 of 40 cases and arthralgia in a further 4. In KEIL's view[9] pain which seems to be situated near a joint is likely to be due to lesions in adjacent muscles, tendons, or subcutaneous tissue, and deformity (found most often in the elbows, knees, hips, and fingers) to fibrosis of these tissues. Pathologists have seemed incurious about joints, and DOMZALSKI and MORGAN could find no description of the histology of joints in dermatomyositis.

The ætiology of dermatomyositis is at least as obscure as that of any of the collagen diseases, but in recent years attention has been focused on the rather striking incidence of carcinoma in patients with the disease. This association was recognised twenty years ago by BEZECNY.[10] FORMAN[11] and PROSSER THOMAS[12] described further cases in this country, and others have been recorded in the United States. DOMZALSKI and MORGAN collected accounts of 51 patients with dermatomyositis and carcinoma; the site of the neoplasm did not seem to be material.

Treatment remains empirical and unsatisfactory. As we said in a recent leading article[13] the response to cortisone is neither consistent nor dramatic, but the disease can certainly be modified to some extent by corticotrophin or cortisone,[14–17] and the hazards of hormone therapy may have to be accepted in seriously ill patients. These hazards included gastric ulceration and hæmatemesis in 1 of the cases treated by DOMZALSKI and MORGAN and an acute psychosis in the other. Tocopherols may decrease creatine excretion,[18] but the therapeutic effects claimed for these substances[19] and for potassium *p*-aminobenzoate[20] have not been confirmed. Palliative

1. Domzalski, C. A., Morgan, V. C. *Amer. J. Med.* 1955, **19**, 370.
2. Keil, H. *Ann. intern. Med.* 1942, **16**, 288.
3. O'Leary, P. A., Waisman, M. *Arch. Derm. Syph., Chicago*, 1940, **41**, 1001.
4. Griffiths, W. J. *Brit. J. Derm.* 1940, **52**, 295.
5. Beard, H. H. Creatine and Creatine Metabolism. Brooklyn, 1943.
6. de Morsier, G., Feldmann, H., Argand, J., Wissmer, B. *Mschr. Psychiat. Neurol.* 1952, **123**, 97.
7. Anderson, T. E. *Brit. J. Derm.* 1952, **64**, 71.
8. Jager, B. V., Grossman, L. V. *Arch. intern. Med.* 1944, **73**, 271.
9. Keil, H. *Ibid*, 1940, **66**, 339.
10. Bezecny, R. *Arch. Derm. Syph., Berlin*, 1935, **171**, 242.
11. Forman, L. *Brit. med. J.* 1952, ii, 911.
12. Prosser Thomas, E. W. *Ibid*, 1953, i, 101.
13. See *Lancet*, Nov. 19, 1955, 1071.
14. Thorn, G. W., et al. *New Engl. J. Med.* 1950, **242**, 824.
15. Oppel, T. W., Coper, C., Michorat, A. T. *Ann. intern. Med.* 1950, **32**, 318.
16. Lever, W. F. *New Engl. J. Med.* 1951, **245**, 359.
17. Andrews, G. C. *Arch. Derm. Syph., Chicago*, 1951, **64**, 218.
18. Millharat, A. T., Toscani, V., Bartels, W. E. *Proc. Soc. exp. Biol., N.Y.* 1945, **58**, 40.
19. Burgess, J. F. *Lancet*, 1948, ii, 215.
20. Zarafonetis, C. J. D., Curtis, A. C., Gulick, A. E. *Arch. intern. Med.* 1950, **85**, 27.

treatment in the final stages may have to include a respirator and tube-feeding. In general the prognosis is poor. Deterioration may be arrested by spontaneous remission, but at least half the patients die from the disease and the average duration of survival is two years.[21]

## The Ureter

THE anatomy of the ureter gives little clue to the complexity of its function. It increases in thickness as it runs from the kidney to the bladder, partly by addition of a third outermost layer of longitudinal muscle, and partly by an increase in bulk of the two deeper muscle layers. In the empty organ the epithelial lining lies in folds which open out as the ureter fills. Cross-sections of the fully filled ureter show that the lumen is narrowest at the bladder end where the muscle bulk is greatest. This structural pattern is common to many species, such as man, dog, cat, rat, sheep, pig, and buffalo; so it has clearly not developed after man assumed an upright posture, though it may have been one of the factors making this posture possible. Pharmacologically the nerve-supply is both sympathetic and parasympathetic, but anatomically it is hard to be dogmatic. Whatever their source, once the nerves reach the ureter they form a network along its whole length under the outer fibrous coat[22]; and a second network has been described in the submucosa.[23] Most workers agree that ganglion cells are to be found in the ureter, large groups of them at the lower end, smaller groups at the upper, and perhaps along the whole length as well.[23]

The usual, and perhaps too readily accepted, belief is that as urine is formed it is swept by peristaltic waves straight down to the bladder, that the strength and speed of the waves depend on the rate of urine flow, and that continued back-pressure or obstruction may cause dilatation or atony of the ureteric muscle. The peristalsis is believed by some to be controlled by the central nervous system and by others to depend on local factors. The use of sympathomimetic or parasympathomimetic drugs suggests that peristalsis is locally controlled but that tone is regulated centrally, perhaps by some reflex originating in end-organs in the bladder or ureter itself. Tonic contraction seems to be largely a function of the lower half of the ureter.[24] Clearly, the ureters must have a fair degree of independence since many experimental observations have been made on the movements of the isolated organ, either perfused or suspended in a bath of Ringer-Locke solution. Moreover, a quiescent isolated ureter can be made to contract rhythmically by distending it with a solid body such as a bead or with fluid, when the vigour of peristalsis depends on the head of pressure of the perfusion fluid.[25] Several workers have compared the behaviour of the upper, middle, and lower portions of the ureter. Satani[26] noticed that the renal end showed small contractions at a faster rate than the other parts; the middle portion contracted most powerfully and slowly; and the bladder end gave small slow contractions. The belief was that the upper end normally served as pacemaker, though the ureter could develop antiperistalsis if it was treated with adrenaline or perfused from the lower end.[27] On the other hand, antiperistalsis has not been seen in the intact organ.[24] Recent work[24 26] confirms SATANI's findings on the activity gradient and brings out some other interesting points. Pressure records were obtained from ureters of various animals by thrusting hypodermic needles attached to strain-gauge manometers into the ureteric lumen; in this way the passage of fluid from kidney to bladder was uninterrupted.[24 25] Two patterns of ureteric activity were observed superimposed on minor species and individual differences: in one, a regular series of peristaltic waves originating at the upper end of the ureter caused a rise of pressure at successive needle points, with a return to basic level between waves; in the other, each of a regular series of waves in the top section produced only a small peak and a slight rise of pressure further down the ureter—i.e., the waves faded out before reaching the bladder. When the basic pressure in the lower part reached a certain level a large contraction occurred in this part, following which the basic pressure fell, and the pattern was then repeated. Thus, ureteric flow might show a through or a segmental pattern. In the segmental pattern, the upper reaches of the ureter pushed urine into a pool in the lower part; when this pool was large enough to stimulate the ureteric muscle by distension, it was discharged in whole or part into the bladder. Even when bladder pressure was increased, the strong muscle at the lower end of the ureter was capable of discharging urine, by a process of more powerful peristalsis and a rise in basic pressure. Man regularly needs this power, and so do animals in any attitude in which the pelvis is lower than the rest of the abdomen. When man stands or sits his abdominal contents press on the bladder and raise its pressure to as much as 20–40 cm. water.[28] That this is a true rise in intravesical pressure and not merely a rise in intra-abdominal pressure is shown by the fact that in these circumstances intragastric pressure falls. All workers who have tried it agree with GALEN's old observation that it is very difficult to force fluid back into the ureter from the bladder, because the simple flap at the ureteric orifice and the oblique passage of the ureter through the bladder wall form a highly efficient valve.

It seems then that through-peristalsis occurs at high rates of urine flow. At slow rates, flow in the ureter is segmental with pooling at one or more sites. At intervals the whole or part of a pool moves on to the next pool or into the bladder itself.[24] The flow is also segmental when bladder pressure is high, since the pooling, by stretching the ureteric muscle, enables it to do more work. An interesting observation was that on raising bladder pressure by compression the basic pressure in the lower part of the ureter increased, but that this increase was not transmitted to the renal end, and that a constriction might be maintained between the upper pool and a vigorously contracting lower one, so that the back-

21. Hollander, J. L. Arthritis and Allied Conditions. London, 1953.
22. Engelmann, T. W. *Pflüg. Arch. ges. Physiol.* 1869, **2**, 243.
23. Gruber, C. M. *Physiol. Rev.* 1913, **13**, 497.
24. Gould, D. W., Hsieh, A. C. L., Tinckler, L. F. *J. Physiol.* 1955, **129**, 436.
25. Gould, D. W., Hsieh, A. C. L., Tinckler, L. F. *Ibid*, p. 425.
26. Satani, Y. *Amer. J. Physiol.* 1919, **49**, 474.
27. Gruber, C. M. *J. Urol.* 1928, **20**, 27.
28. Gould, D. W., Hsieh, A. C. L., Tinckler, L. F. *J. Physiol.* 1955, **129**, 448.

ward flow of urine was prevented and the nephrons protected.[24] This protective function of the ureter is hinted at by measurements of renal pelvic pressure. At low rates of urine flow this is zero or even slightly negative[29]; at very high rates the pressure rises only a little and then flattens out, since the formed urine passes down the ureter in a continuous stream.[30]

The work that has been done on animals can probably be applied in full to man, and cineradiography may be a means of confirming this point.[31] TRATTNER [11] designed an apparatus whereby he could record flow and pressures from the ureters in man; and, allowing for the difficulties and inaccuracies inevitable in such observations, the pressure patterns and type of flow agree well with those found in animals. Not everyone believes that the through type of flow is the only normal one in man. BEGG [33] has noted how often the X-ray appearances are consistent with the segmental or cystoid [34] type of flow; and he pointed out that this should by no means be considered abnormal. It must be remembered that pyelography is usually performed when the patient is somewhat dehydrated and has a slow rate of urine flow. According to the work of GOULD et al., segmental flow would be expected and normal in such conditions. Thus, many of the variations seen in pyelograms are physiological or compensatory and reversible phenomena, and not a sign of disease.

29. Lucas, D. R. *Amer. J. Physiol.* 1908, **122**, 243.
30. Morales, P. A., Crowder, C. H., Fishman, A. P. *J. Urol.* 1952, **67**, 484.
31. See *Lancet*. Nov. 12, 1955, p. 1042.
32. Trattner, H. R. *J. Urol.* 1932, **28**, 1.
33. Begg, R. C. *Brit. J. Urol.* 1946, **18**, 176.
34. Fuchs, F. *Z. urol. Chir.* 1936, **35**, 169.

# Annotations

## TOO EARLY RETIREMENT

To be unable to find work when one is still fit and able is both a personal tragedy and a waste of the community's resources; so it is encouraging to learn, from the second report of the National Advisory Committee on the Employment of Older Men and Women,[1] that more work is now being found for the aged. The shortage of labour generally has certainly acted as a spur to industry to find suitable jobs for the older unemployed, but the publicity given to the first report [2] of the National Advisory Committee has also played a part.

Unobtrusively the reasons for employing the aged have become more social and less economic. More information is now available about the trends of population; and it is noteworthy that, whereas the first report estimated that between 1951 and 1977 the number of "producers" would remain much the same while the number of retired people over minimum pension ages would increase by about $2^1/_2$ million, the second report talks of an increase of over a million in the number of producers by 1979, against an increase of only about 2 million retired people.

Discussing the inquiry made into the reasons that lead people to retire or stay at work after pensionable age,[3] the committee point out that about a quarter of the men studied were retired or discharged by their employers. Such retirement is due more to the custom or pension arrangements of the occupation than to any careful assessment of the ability of the worker to carry on. "No doubt there were many who might have continued to give efficient service in their old jobs among familiar surroundings and work-mates and with an employer they knew, who would not have felt able to face work in a new environment." About half the men and women retiring at minimum pension age did so for health reasons, but the majority of these did not have serious records of sickness. Their reason, in fact, was often not based on medical evidence; it was subjective.

The emphasis of the present report is on propaganda and research. Research is clearly needed in each *firm* to find work opportunities for the older worker, and the committee conclude that industry generally ought also to promote research, though they do not say who is going to finance it. Much useful investigation of ageing is being undertaken at present under the auspices of the Nuffield Foundation, the Medical Research Council, and other bodies; but one subject which is not, we think, receiving attention and clearly deserves it is "subjective ill health." Much more information is needed about the high proportion of men who complain of ill health and have little objective record of it. This problem of *social* medicine must not go by default.

1. Cmd. 9628. London: H.M. Stationery Office. 1955. Pp. 28. 1s. 9d.
2. Cmd. 8963; see *Lancet*. 1953. ii, 871.
3. See *Lancet*, 1954, ii, 1167.

## ALLERGY AND ENCEPHALOMYELITIS

THE precise way in which demyelination is brought about in the nervous system is unknown, except perhaps in the postvaccinal type of encephalomyelitis. The procedures which can start demyelination in experimental animals have been reviewed by Wolf.[1] They include the repeated injection of heterologous or homologous brain emulsions with or without adjuvants. The lesions so produced are disseminated and perivenular, and predominantly in the white matter. As well as demyelination, there is proliferation of adventitial cells and sometimes of microglia. Encephalitis due to arsphenamine [2] or following streptomycin and *p*-aminosalicylic acid [3] is possibly the result of hypersensitivity. The similarity of the features in experimental animals to those in acute disseminated encephalomyelitis and acute hæmorrhagic leucoencephalitis in man suggests that these conditions are allergic. In acute disseminated encephalomyelitis areas of perivascular demyelination show no inflammatory cells and there is little evidence of nerve-cell destruction; some perivascular cuffs of lymphocytes are present and petechiæ are occasionally found. Reviewing the literature, Crawford [4] states that multiple capillary hæmorrhages and fibrin impregnation of the vessel walls are characteristic of hæmorrhagic leucoencephalitis.

Russell [5] believes that these two conditions are variants of one pathological process. She describes an example of hæmorrhagic leucoencephalomyelitis with typical history and distribution of lesions but scanty hæmorrhagic foci, and a case of acute disseminated encephalomyelitis showing greatest damage in the brain stem and spinal cord, with hæmorrhage visible to the naked eye. She also notes fibrinoid degeneration of the vessels in hæmorrhagic leucoencephalitis and a polyarteritis-nodosa type of arteriolar lesion in acute disseminated encephalomyelitis. Russell's view suggests that the two diseases differ principally in the violence with which a common agent attacks the central nervous system—a concept which receives support from other workers. Marshall and White [6] studied the reactions of the reticular tissues of rabbits to various antigens; they found that

1. Wolf, A. 1st Internat. Congr. Neuropath. Rome, 1952; vol. 1, p. 121.
2. Russell, D. S. *J. Path. Bact.* 1937, **45**, 357.
3. Cavanagh, J. B. *J. clin. Path.* 1953, **6**, 128.
4. Crawford, T. *Ibid*, 1954, **7**, 1.
5. Russell, D. S. *Brain*, 1955, **78**, 369.
6. Marshall, A. H. E., White, R. G. *Brit. J. exp. Path.* 1950, **31**, 157.

plasmablasts appeared in the spleen within a few days, and if repeated injections of antigen were given, immature and later mature plasma-cells accumulated. Campbell and Good [7] observed similar changes in the spleen in guineapigs with encephalitis due to sensitisation to homologous brain tissue. Russell describes the development of foci of plasma-cells and their precursors in the spleen in both acute hæmorrhagic leucoencephalitis and acute disseminated encephalomyelitis, and she argues from these findings that the two conditions are nosologically one and that allergy is the basis of the reaction in the central nervous system.

## REGIONAL ILEITIS

FROM every aspect regional ileitis is hard to treat. The time was when Crohn's disease was excised as soon as revealed, but hard facts culled from efficient and persistent follow-up have altered our approach. At the Mayo Clinic,[8] the recurrence-rate following operation on 270 patients was 37% at two years, rising to 80% at fifteen years. In this country Cooke,[9] describing a series of 90 patients, 83 of whom were operated on, found recurrences in 45% at two years and 78% at ten years. Only a few of these recurrences were disclosed by routine X-ray examination in patients free from symptoms. Resection cannot therefore be regarded as a cure. Indeed a difficulty arises as soon as resection is contemplated, for any attempt at eradication calls for wide resection because there are shallow ulcers confined to the superficial layers of the mucosa at considerable distances beyond areas of obvious thickening, and no clue to their presence and situation may be found on the serosal surface of the gut.[10] Even extensive resection becomes ineffective if it does not include all "aphthoid" ulcers, which can conceivably be the starting-point of recurrence. The trouble is that these patients are prone to steatorrhœa (it was present in 45 out of 57 patients investigated by Cooke) and resection aggravates this. It therefore seems that surgery has no place in cure but must be reserved for certain complications, the most important of which is obstruction, if only because it is the most common. Even this decision calls for nice judgment since obstruction is by no means always the outcome of simple stenosis; indeed a frank localised stricture is rare and usually follows healing. More commonly a length of intestine is rendered immobile by thickening and œdema, but retains a lumen through which alimentary contents are propelled vis-à-tergo. But the propulsive force from the normal intestine above is lost with potassium depletion; the total exchangeable potassium may fall to one sixth of normal, due to chronic depletion by diarrhœa. Under these circumstances the normal intestine becomes distended and atonic. Potassium must therefore be restored before a decision is made to excise an area of ileitis which appears to be provoking obstruction.

Internal fistulæ and failure to thrive after proper medical care are further indications for operation, but while surgery can offer no cure there is also no specific medical remedy. We rely on rest, aided by restoration of body-fluids and chemistry. Cooke emphasises the need for protein (low serum-albumin levels are not uncommon) and potassium, the depletion of which, apart from its effect on somatic and plain muscle, may cause mental confusion. The value of corticoids remains unproved, but it seems that they can induce remissions in children and in early or acute cases. Their place in chronic disease comes after resection when a maintenance dose may put off the evil day of recurrence. But Cooke's first rule of treatment is that all patients must remain under regular medical supervision so that recrudescence can be countered before biochemical changes have gone too far.

7. Campbell, B., Good, R. A. *Arch. Neurol. Psychiat.* 1950, **63** 298.
8. Van Patter, W. N., Bargen, J. A., Dockerty, M. B., Feldman, W. H., Mayo, C. W., Waugh, J. M. *Gastroenterology*, 1954, **26**, 347.
9. Cooke, W. T. *Ann. R. Coll. Surg. Engl.* 1955, **17**, 137.
10. Brooke, B. N. *Lancet*, 1953, **i**, 1220.

## BABIES' MEDICINE

AN inquiry was lately carried out by Bryant [1] to determine how often parents give medicines to their children without medical advice; to assess the frequency of infants' visits to family doctors and welfare centres; and to see how far additional vitamin foods were used. A representative sample of families with children under twelve months were interviewed by health visitors. Only 8 out of 503 infants had not been given an unprescribed medicine during the first year; three-quarters had been taken to the family doctor at least once; 1 in 6 had attended hospital outpatients or been admitted; half were "regulars"—i.e., known attenders—at the welfare centre, and another fifth "occasional" attenders. Social class seemed to make no difference as far as attendance at the family doctor was concerned, but welfare-centre attendances were less frequent in families in the lower part of the social scale. On the other hand, children in the less well-to-do families were taken to hospital more often. This confirms the Newcastle experience [2] that the mothers and families of semi-skilled and unskilled workers use welfare centres less than others but attend hospital more often; one reason is that infants in these families are more likely to have serious infections. In the Newcastle survey in 1947–48, there was also no indication of social-class difference in the number of times the doctor was called, but there was evidence that he was called for a smaller proportion of illnesses in poorer families. But it is apparent that today most infants are seen either by family doctors or welfare centres at some time in the first year and that half of all infants who see their family doctor do so more than once. This in turn is additional evidence, if any be needed, of the need of the family doctor for pædiatric training and experience.

Unprescribed medicines or applications were given on occasion to almost every infant, and there was no difference in this habit between the social classes. A wide variety of substances were given: cough medicine, sleeping medicine (aspirin was commonly given for this purpose), aperients, and boracic acid or ointment for napkin rashes: and many children had glycerin, borax and honey, or gentian-violet applied to their mouths. Surprisingly few mothers seemed to rub the child's chest, and camphorated oil was not even mentioned. Most of these home treatments seemed to be given only once or twice, and only a very few children received "regular" medicine other than aperients; and even these were given regularly to only 1 in 8 infants ("aperients" presumably includes all mild laxatives). It would have been interesting to know how many infants received more than one type of medicine regularly and how this correlated with the standards of maternal care.

As Bryant observes, many (and perhaps most) of the substances given are almost certainly harmless; but he recalls the sinister story of pink disease and mercury teething-powders, and no-one can be entirely happy about home treatment with boracic acid.[3] Nevertheless it would be wrong to deny the mother simple medicines or blame her if she sometimes follows, without asking, the common teaching of welfare centres. But the facts that Bryant records go further: there is cause for satisfaction that several disturbing practices of earlier days are declining; thus, alcohol was given to only 1 infant, and gripe-water, "cinder" water, and "tar" water are not mentioned, nor is breast milk for conjunctivitis.

1. Bryant, H. *Med. Offr*, 1955, **94**, 209.
2. Spence, J., Walton, W. S., Miller, F. J. W., Court, S. D. M. A Thousand Families in Newcastle upon Tyne. London, 1954.
3. See *Lancet*, 1954, **i**, 507.

Nearly 10% of the infants did not get cod-liver oil added to their food, as the orthodox teaching of pædiatric and welfare practice demands; so in this respect these mothers were falling short of accepted standards. But in this country today vitamin-D-deficiency rickets is rare, and an interesting comparison has been made in Salford [4] of two groups of children in their second year of life. One group received regular cod-liver oil additions daily for at least six months before examination, but the other group had no cod-liver oil other than in dried milk or infant cereals. There were no differences in bone growth or serum alkaline-phosphatase and no radiological evidence of rickets in either group. There was a difference in body-weight and height, probably reflecting the difference in care and diet. It seems that the vitamin D added to dried milk and infant cereals is enough to prevent rickets at least in the first and second years in full-term children, and that when children are receiving the additional cod-liver oil, they may be having too much of the vitamin. And this excess may be concerned in the production of hypercalcæmia and renal acidosis in infancy.[5]

Bryant's investigation is a good example of the small yet pertinent comment on contemporary habits which this part of the National Health Service can readily make.

## VENO-OCCLUSIVE DISEASE OF THE LIVER

Most cases of the rare Chiari's syndrome seen in this country are due to occlusion of the main hepatic veins or of the inferior vena cava at the level of the caval fossa.[6] A much commoner form of the syndrome, however, has recently been reported from Jamaica as serous hepatosis,[7] or veno-occlusive disease of the liver.[8]

Three stages of the disease can be fairly easily defined. In the acute stage, occurring almost exclusively in children between 18 months and 3 years of age, the abdomen enlarges rapidly owing to hepatomegaly, with or without ascites. Gastro-intestinal and other symptoms are mild, but liver-function tests are almost always abnormal. Recovery is usually rapid, even without treatment, but in a few patients hepatomegaly persists, and recurrent ascites necessitates repeated paracenteses. This is the subacute phase. The third or final stage is seen in older children, and clinically is indistinguishable from hepatic cirrhosis with pronounced features of portal hypertension.

The lesion underlying this variant of Chiari's syndrome is an occlusion of the hepatic veins, but the vessels involved are almost exclusively the sublobular and centrilobular veins, the larger branches being rarely affected. The principal change is an obliterative endophlebitis, and thrombosis is not important. The intima is at first greatly swollen by œdema, and then concentric fibrosis completely occludes the affected segment. Intense hepatic congestion results and there is wide dilatation of the sinusoids and atrophy and necrosis of the parenchyma. A progressive fibrosis replaces the destroyed liver cells. The picture at this stage resembles cardiac cirrhosis. Progression of the fibrosis, however, ultimately obliterates the normal lobular architecture, and the final picture closely resembles Laennec cirrhosis, except for the characteristic obliterative endophlebitis.

Little definite is known of the cause of this important liver disease. Malnutrition, of fundamental importance in other forms of liver injury, does not seem to be primarily to blame, and patients in the acute phase recover as readily on a high carbohydrate diet as on one rich in protein.[8] This suggests that the benefit of hospital treatment might be largely due to withdrawal from some toxic agent in the ordinary environment. Attention has been particularly drawn to the great popularity of bush teas in areas where veno-occlusive disease is common. Most of these vegetable infusions are probably harmless, but it is known that a condition closely resembling veno-occlusive disease occurs in man following the accidental consumption of senecio (ragwort).[9] Similar hepatic damage has also been produced in laboratory animals by senecio feeding or by injection of retrorsine, one of the alkaloids extracted from senecio by Davidson[10] in 1935. The possible toxicity of the bush teas is now being closely studied in many parts of the world. If a poison is found, there should follow a highly rewarding chapter in preventive medicine.

## THYROID CANCER AFTER RADIOTHERAPY

In 1950 Duffy and Fitzgerald[11] investigated the past history of 28 patients with thyroid cancer, all of whom were under the age of 18. They found that no less than 10 of them had received X-ray treatment, directed at the thymus, between the ages of 4 and 16 months. Simpson and others[12] followed up 1400 children who had received X-ray therapy to the thymic region, and they found that the incidence of thyroid cancer was much higher in the treated group than in their untreated siblings. Clark[13] has now reported a further series of 13 children with thyroid cancer, seen in Chicago during the past 6 years. Every one had previously been treated with X rays, either for thymic enlargement, cervical adenitis, enlarged tonsils, bronchitis, or pertussis. The interval between irradiation and the diagnosis of thyroid cancer varied from 3 to 10 years, the average being 6·9 years. The tumours were all well differentiated, but all except one had spread outside the thyroid. Buckwalter[14] reports that 8 children under 15 with thyroid cancer were seen at the University of Iowa Hospitals in the past five years, and 3 of them had had irradiation for an enlarged thymus in infancy.

These reports appear to establish beyond reasonable doubt that irradiation of the thyroid region during infancy can cause cancer in later childhood. Clark remarks on the recent big increase in reported cases of thyroid cancer in children and suggests that it can be attributed to the great popularity of X-ray treatment to the neck and upper chest in infancy during the period 1930–45. The principal indications for this treatment were supposed thymic enlargement and cervical adenitis. This type of treatment was probably used less here than in America, but nevertheless a survey of the situation in this country seems called for. Meanwhile, it should be emphasised that no infant ought to be exposed to therapeutic doses of X rays unless a malignant condition is already present.

In Clark's series the interval between irradiation and the diagnosis of thyroid cancer was about 7 years. If this relatively short "incubation period" can be applied to adult patients with thyrotoxicosis treated with radio-iodine, then it is encouraging to learn from Chapman and Maloof's authoritative review[15] that no cases of cancer have as yet appeared following this treatment. Radio-iodine was first given therapeutically in 1941 and by 1945 it was in wide use in the United States. If this treatment were as carcinogenic in adult life as X rays appear to be in infancy, then at least a few cases of thyroid cancer following radio-iodine therapy should have been reported by now.

4. Berry, W. T. C., Boyes, K. M. B. *Mon. Bull. Minist. Hlth Lab. Serv.* 1955, **14**, 162
5. See *Lancet*, 1954, ii, 127.
6. *Ibid*, 1955, i, 710.
7. Hill, K. R., Rhodes, K., Stafford, J. L., Aub, R. *Brit. med. J.* 1953, i, 117.
8. Jelliffe, D. B., Bras, G., Stuart, K. L. *Ann. trop. Med.* 1954, **48**, 386.
9. Selzer, G., Parker, R. G. F. *Amer. J. Path.* 1951, **27**, 885.
10. Davidson, J. *J. Path. Bact.* 1935, **40**, 285.
11. Duffy, B. J. jun., Fitzgerald, P. J. *Cancer, N.Y.* 1950, **3**, 1018.
12. Simpson, C. L., Hempelmann, L. H., Fuller, L. M. *Radiology*, 1955, **64**, 840.
13. Clark, D. E. *J. Amer. med. Ass.* 1955, **159**, 1007.
14. Buckwalter, J. A. *J. clin. Endocrin.* 1955, **15**, 1437.
15. Chapman, E. M., Maloof, F. *Medicine*, 1955, **34**, 261.

# Special Articles

## DOMICILIARY CONSULTATION IN PSYCHIATRIC PRACTICE

### ANALYSIS OF 1000 VISITS

DENIS LEIGH
M.D. Manc., F.R.C.P.
PHYSICIAN, BETHLEM ROYAL AND MAUDSLEY HOSPITALS, LONDON

THREE years ago I reported my experiences in the domiciliary visiting of psychiatric patients (Leigh 1952). Since then, I have completed my thousandth visit. In view of the somewhat uninformed enthusiasm over the "Amsterdam experiment," it is opportune to re-examine my findings in the light of greater experience. Recapitulating my earlier conclusions, domiciliary visiting is an important advance in three respects:

1. The patient is seen in his own social setting, in a friendly, informal atmosphere. His fears and prejudices against psychiatry and psychiatrists are allayed by this first contact in the home, and in 90% of the patients, treatment or advice became possible on an entirely voluntary basis.

2. The visit does much to bring the family doctor more closely into the hospital orbit, and at the same time help him in a field where his education has often been defective.

3. The psychiatrist is brought sharply into a world of practicality. Practising a branch of medicine in which indecision is often curative, and of less harm to the patient than decision, he is forced to decide certain issues there and then. His knowledge of general medicine is also tested, for 20% of the patients proved to be suffering primarily from physical diseases.

Arising from the domiciliary visit, a special relationship was developed with certain general practices. The four partners of one of these practices collaborated in a further study of the patterns of psychiatric illness in general practice (Bodkin et al. 1953). About 1 patient in every 140 on the list of this practice was referred to me over the period of a year; but, considering that in Fry's practice neurosis was among the most frequent causes of attendance (Fry 1952), this proportion is reasonably low.

In Amsterdam, what is essentially a domiciliary service has been built up over the past twenty years under the direction of Prof. A. Querido (Querido 1935, 1948-49, 1950). In 1954, through his kindness, I spent a short time studying the work of the Amsterdam service at first hand. The supporters of preventive psychiatry have been quick to realise the potentialities of the Amsterdam service, and much enthusiasm has been aroused; but, to the best of my knowledge, there is little statistical information from this service. I have therefore analysed experiences of very similar work in England.

### Technique of Domiciliary Consultation

Experience has confirmed that a general practitioner prefers to contact the consultant directly with a request for a visit, rather than through a domiciliary bureau. A clerical service dealing with requests for visits is essential, so that adequate records may be kept and there is as little delay as possible between the request and the visit. Practitioners do not always assess correctly the urgency of a patient's condition; so if possible a visit is carried out on the day the request is received.

For preference, the patient is visited alone, the family doctor being consulted before or after the visit. Psychiatric patients often reveal to the psychiatrist information which they withhold from the family doctor.

The ethics of the consultation, however, differ in no other way from those of other consultations. The family doctor is always regarded as the person in charge of the patient, and no patient is seen except on his request. In Amsterdam, on the other hand, the visit may be made at the request of the police, a neighbour, or a member of the family, although it is said that the family physician is always informed.

Full notes must be taken, and a special printed sheet has been devised to fit in with the hospital record system.

### *Disposal of Patients*

Suitable disposal is the keynote of successful domiciliary visiting, and the physician making the visit must have both outpatient and inpatient facilities available to him.

Table I shows the disposals of all cases during the past six years. The pattern varies little from year to year, and shows that about 90% of the patients were voluntary,

TABLE I—NUMBER OF PATIENTS VISITED AND TREATMENT RECOMMENDED

| Disposal | 1949 | 1950 | 1951 | 1952 | 1953 | 1954 | Total |
|---|---|---|---|---|---|---|---|
| Total | 93* | 153 | 181 | 199 | 201 | 184† | 1011 |
| To observation ward | 8 | 23 | 12 | 19 | 27 | 23 | 112 (*11%*) |
| Inpatient | 31 | 50 | 60 | 59 | 41 | 38 | 279 (*28%*) |
| Outpatient | 24 | 44 | 62 | 74 | 78 | 57 | 339 (*33%*) |
| Advice to G.P. or family | 18 | 27 | 32 | 35 | 35 | 50 | 197 (*20%*) |
| To mental hospital as voluntary patient, or to general hospital | 9 | 9 | 15 | 12 | 20 | 10 | 75 (8%) |
| Treatment in day-hospital | .. | .. | .. | .. | .. | 5 | 5 (*0·05%*) |

* Including 3 repeat visits.
† Including 1 patient who died shortly after the visit.

and over 50% were treated as outpatients. If day-hospital facilities had been available before 1954, and if our day-hospital had been larger, the proportion treated as outpatients, would be higher still.

During this period there was no successful suicide, or an attempt seriously endangering life. Perhaps this was due to the close contact between psychiatrist and family doctor, and the psychiatrist's control of hospital beds.

In Holland, the family doctor cannot admit directly to a hospital; the intervention of the psychiatric service is always necessary, and as the aim of the service is to keep patients out of hospital, this is indeed essential.

Diagnoses in these cases also show a remarkable uniformity from year to year (table II). I did not keep

TABLE II—DIAGNOSES IN DOMICILIARY PSYCHIATRIC PRACTICE

| Diagnosis | 1951 | 1952 | 1953 | 1954 | Totals (%) |
|---|---|---|---|---|---|
| Depressive reaction | 67 | 65 | 64 | 69 | 34 |
| Neurotic reaction | 54 | 59 | 54 | 56 | 28 |
| Organic reaction | 24 | 42 | 42 | 28 | 19 |
| Schizophrenic reaction | 14 | 15 | 18 | 13 | 8 |
| Senile reaction | 12 | 21 | 13 | 12 | 8 |
| Others | 10 | 2 | 4 | 6 | 3 |

records in the years 1949–50, but there is no reason to believe that the pattern differed then.

Studies by Watts and Watts (1952) and by Fry (1952) in their general practices confirm that the two most important psychiatric problems for the family doctor are depressions and neuroses. Watts and Watts analysed three years work in a Leicestershire practice and found that depressive reactions comprised 36, 36, and 31% of the psychiatric patients during 1948, 1949, and 1950 respectively. Fry found that the majority of his psychiatric patients were "involutional" women.

Depression is so common, the suicidal threat so disturbing, and the prognosis of a properly treated depression so good that the family doctor must be conversant with all aspects of this disorder.

The neurotic disorders form a comparatively large proportion of "acute" cases. Psychiatrists recognise that special techniques and facilities are necessary to treat the neuroses effectively, and general practice is

not the milieu in which to practise psychotherapy, except through a benign, paternal relationship. Adequate psychotherapeutic and other facilities must be available if neurotic patients are to be helped, and the development of outpatient and day-hospital services has been invaluable.

Organic disorders comprise nearly a fifth of the cases, and the psychiatrist must have a sound training in general medicine, with a particular knowledge of neurology.

The more uncommon effects of a cerebral vascular lesion, such as aphasia, are often misinterpreted as "hysteria," and even very experienced doctors may be misled by a physical condition presenting as a mental disturbance; this is particularly so with delirious reactions.

Organic illness is often a particular problem for the psychiatrist. When the family doctor calls for a domiciliary visit on a "hysterical" or "difficult" patient, and the psychiatrist diagnoses cerebral tumour, strong feelings are often evoked, and in some cases, the practitioner never calls out the psychiatrist again.

### General Practitioners Referring Patients

About half of the doctors referred only 1 patient a year, and most of the patients were referred by comparatively few practitioners (table III). Thus, I made

TABLE III—NUMBER OF DOCTORS REFERRING PATIENTS

| — | 1949 | 1950 | 1951 | 1952 | 1953 | 1954 |
|---|---|---|---|---|---|---|
| Total no. of doctors referring | 58 | 63 | 79 | 79 | 79 | 77 |
| *No. of doctors referring:* | | | | | | |
| 1 patient .. .. .. | 45 | 37 | 49 | 39 | 41 | 41 |
| 2–5 patients .. .. | 11 | 22 | 23 | 33 | 31 | 30 |
| 5–10 patients .. .. | 1 | 2 | 5 | 6 | 4 | 6 |
| Over 10 patients .. .. | 1 | 2 | 2 | 1 | 3 | 0 |

201 visits in 1953 and saw 160 new patients, who were referred by 38 of the 79 doctors who called me in consultation.

Blacker (1948) pointed out that between 1938 and 1942 there was an increase in the number of neurotic patients seen at 216 psychiatric clinics in England and Wales. He felt that this was probably due to a growing use of the country's psychiatric facilities by the family doctor, and was somewhat alarmed at the prospect of "a descent in vast multitudes" of neurotic patients upon the psychiatric clinics should the family doctor become "psychiatry conscious." At the time of his survey, however, it was not possible to analyse the patterns of psychiatry in general practice. Blacker has now analysed the referrals by general practitioners to the Maudsley Hospitals, and he finds that 42% of the doctors referring psychiatric patients sent only 1 patient annually to the hospital, and that half of our patients came from only 10% of the doctors (C. P. Blacker, personal communication).

My own outpatient work during 1952 confirms these findings. Of 223 new patients 196 were referred by 90 doctors; the remaining 27 came from other sources.

All these doctors were known to me; all patients were referred personally; and no other hospital was used by the doctors. Yet a small proportion (15%) of the 90 referred about half the patients. It is strange that out of a busy practice of 2000–4000 patients, only 1 patient per year reaches a psychiatric hospital, and it seems that the general practitioner himself deals with most of his psychiatric patients. Fry (1952) saw 570 psychiatric patients during 1951, and Watts and Watts (1952) stated that 12% of their patients were "functionally ill."

### *Undergraduate and Postgraduate Teaching*

I believe that these figures do not show that general practitioners are well skilled in psychiatry, but rather the reverse, and that they reflect inadequate teaching in the past, for which psychiatrists can only blame themselves. The present generation of practitioners is almost entirely untrained in psychiatry; a visit to a mental hospital and six or so lectures on mental disease comprised his student education.

What should our present and future students be taught, and can the established practitioners be given further teaching? Teaching should concentrate on the recognition of common psychiatric conditions.

Of every 3 psychiatric patients seen by family doctors 1 has a depressive illness, and the recognition, course, and treatment of the various forms of such illness should be emphasised again and again. Nearly a third of the psychiatric patients have neuroses, and it is important that these should be recognised, as reactions to current stresses or difficulties. Finally, the organic-reaction illnesses should be thoroughly taught.

There is no reason why this teaching should not be available to both undergraduates and postgraduates. Ill-advised teaching of highly controversial and unsubstantiated psychiatric theory leads inevitably to loose and faulty thinking; as I have previously emphasised (Leigh 1952) the family doctor needs a psychiatry which is medically oriented. It is my experience that a family doctor is well advised to steer clear of psychotherapy, other than simple, supportive measures.

### Preventive Psychiatry

Is it possible to keep patients out of hospital, and to treat them in their own social setting?

It is interesting that in New York, the care of non-psychiatric patients in the home arose out of economic necessity (Bluestone 1954). Bluestone stated: "The home care programme for which I was responsible started with the indigent, where no question of fee arose. On a comparable basis, home care cost less than a quarter of the cost of maintaining a patient inside of the hospital."

The advantages of the home care of psychiatric patients were emphasised by Querido (1948–49) and by Ling (1954). Ling implied that mental health in Amsterdam is better than that in London and suggested that "the first class mental health service" in Amsterdam had something to do with this.

Nothing, in my opinion, could be further from the truth than this statement. Statistical information is difficult to obtain, and these criticisms can only be answered by figures obtained by careful study; my own work is an attempt to remedy this defect. What is needed is, first, a survey of all psychiatric patients for whom admission is required by family doctors, and, secondly, a test of the belief that patients are better treated at home.

Ling (1954) wrote of Amsterdam: "about 40% of all adult psychiatric patients referred to the mental health service are never admitted to hospital, and respond with varying success to handling in home and factory." In my own series over 50% were not admitted to hospital, while in 1954 the figure was over 60%.

### Conclusion

My experiences are probably being duplicated all over the country. The domiciliary service is a really important advance in psychiatry; and it maintains the traditional link between consultant and practitioner.

Apart from the theoretical benefits of treating patients in their own homes, there are the practical considerations of the shortage of hospital accommodation and mental nurses, and the cost of inpatient treatment; any measure which prevents admission to hospital and yet offers the same, if not better, patient care, is clearly worth while.

The next step will be the establishment of a visiting unit, which, with the coöperation of the family doctor, will treat the patient in his home environment.

I am grateful to the board of governors, the Bethlem Royal and Maudsley Hospitals for enabling me to visit Amsterdam, and to Prof. A. Querido for allowing me to carry out domiciliary visiting there.

*References at foot of next column*

## ROYAL COLLEGE OF SURGEONS

### First Provincial Meeting

"THIS sink of infamy and corruption—this receptacle of all that is avaricious, base, worthless, and detestable in the surgical profession, like some other Augean stables, is near the hour of its purification." This broadside, fired by *The Lancet* at the Royal College of Surgeons in 1826[1] in the interest of its members, was on exhibition for the entertainment of fellows and members at Manchester on Dec. 10. No-one attending this first scientific and first provincial meeting ever held by the college could have shared those sentiments. The meeting drew a large attendance of over 500 who were regaled with a scientific exhibition to meet all tastes and interests, and with sumptuous hospitality.

There were 44 separate sections to the scientific exhibition, set out and displayed to great advantage on screens set up in the outpatient and neurosurgical departments of the Manchester Royal Infirmary. The morning was devoted to this and to operating sessions. The subjects for exhibition were widely ranged and covered almost every specialty including dentistry; they revealed the results of both clinical and research work. Perhaps the spirit of this exhibition is most aptly indicated by the preface to John Woodall's book *The Surgeon's Mate of Military and Domestic Surgery*, which was on view in the fine collection of old books in the possession of the Manchester Medical Society as a result of Dr. Thomas Windsor's exertions at the end of the last century:

"Discovering faithfully and plainly the method and order of the surgeon's chest, the uses of instruments, the virtues and operations of the medicines, with exact cures of wounds, apostumes, ulcers, fistulas, fractures, dislocations, with the most easy and safest ways of dismembering, the cures of scurvy, of the fluxes of the belly, of the colic and the iliac palsy, of tenesmus and excitus ani, together with a Treatise on the cure of the Plague."

### Malignant Disease

The afternoon was devoted to a symposium on malignant disease, opened by Prof. GEOFFREY HADFIELD, who was concerned with hormone dependence. This may occur in any organ in which normal growth, development, and function are conditioned by an adequate supply of a specific hormone, or hormones acting synergistically. Malignant disease in such organs may depend on the specific hormone, or a synergistic group; in the breast many growths prove to be independent, and of those that are dependent some ultimately become independent. The hormones to which the growth may be subject are either the ovarian œstrogens, the adrenal œstrogens, the adrenal steroids, or those emanating from the pituitary. Professor Hadfield drew attention to examples of hormone-dependent tumours in animals. Foulds's mammary tumour in mice develops only during pregnancy, regresses completely afterwards, and recurs at the next pregnancy; Gardner's testicular tumour in mice is induced by stilbœstrol and maintained by œstrogen, withdrawal of which brings about regression. Experiments have also shown that prolactin, progesterone, and œstrone are synergists responsible for normal duct, alveolar, and lobule development, while the addition of corticotrophin or cortisone together with growth-hormone promotes lactation even in male rats. As regards malignancy, prolactin (a glycoprotein with a molecular weight of 25,000 and thus excretable in the urine) is important, for it is probably identical with urinary mammotrophin excreted in cases of breast carcinoma; alone, prolactin is responsible for the maintenance of breast structure, and experimentally it gains the power to promote normal mammary growth only in company with synergists. Clinically mammotrophin may prove of value in testing whether a particular growth is hormone-dependent or not, since the quantity excreted can be assessed.

Prof. IAN AIRD emphasised the importance of the five-year-cure convention in assessing operable cancer; he also pointed to two defects arising since its introduction—namely, that the emphasis laid upon technical operative detail which characterised surgical discussions in the era before its introduction is being overlooked, and that it has given rise to a competitive desire among individual surgeons to produce ever better five-year results, which accordingly are sometimes misleading. He suggested that there is no certain cure of cancer by radiotherapy or chemotherapy, but only by surgery—and then only in the early case. Cancer of the skin and melanoma can be cured only by early excision; and though results of radiotherapy for carcinoma of the tongue are reasonably good there is always the prospect of recurrence since the lesion has not been excised. Stage-1 carcinoma of the breast is best treated by a modified Halsted mastectomy, which yields a 70–85% five-year survival. Here Professor Aird sounded a note of warning: there is, he declared, little to be gained by bigger operations designed to increase the number of five-year survivors if thereby the operative mortality and the surviving patients' disability are increased. There is a tendency to withdrawal of the surgical offensive; thoracic surgeons no longer regard pneumonectomy as de rigueur for bronchial carcinoma, and lobectomy is now considered adequate in certain cases. Professor Aird applauded this swing to conservatism; carcinoma of the stomach is a case in point; for only a third of the patients come to operation; in a third of these resection is feasible, and a third of these survived for five years—a 3% five-year "cure." With so little prospect of ultimate success it is wrong to do total gastrectomy as a routine, since the operation is bad for the patient. Retreat is the order of the day regarding the pancreas, since total pancreatectomy achieves so little; indeed by contrast he has seen a patient survive for six years after a palliative operation, and another alive seventeen years after Mr. Reginald Vick had short-circuited the bile but had been unable to make any attempt to eradicate the primary lesion and its twelve hepatic metastases. Professor Aird ended by entering a caveat against gross operations for the removal of growth, such as pelvic evisceration.

Sir STANFORD CADE said that the phrase "inoperable cancer" was to patient and relations the worst possible verdict. But this word "inoperable" no longer carries the notion that the patient is beyond treatment; survival can be prolonged. There are no cures in inoperable cancer, no estimations of five-year survivals, but only *control* of the disease, and he wished to establish a new concept—that cancer should be regarded as a condition similar to diabetes, rheumatism, epilepsy, and heart-disease, none of which can be cured but which are well controlled by treatment. Palliation of cancer implies the control of the disease by ablation of the symptoms and signs and a return to near-normal life. If that also leads to a longer life then the sting is taken out of the word inoperable. We must now distinguish

1. *Lancet*, 1825–26, **9**, 558.


DR. LEIGH: REFERENCES

Blacker, C. P. (1948) Neurosis and the Mental Health Service. London.
Bluestone, E. M. (1954) *Brit. med. J.* ii, 887.
Bodkin, J. N., Gaze, R. B., Gomez, G., Howlett, M. S., Leigh, D. (1953) *Ibid*, ii, 723.
Fry, J. (1952) *Ibid*, ii, 249.
Leigh, D. (1952) *Lancet*, i, 915.
Ling, T. M. (1954) *Ibid*, i, 1127.
Querido, A. (1935) *Ment. Hyg., N.Y.* **19**, 177.
— (1948–49) *Soc. Serv., Lond.* **22**, 124.
— (1950) *Folia psychiat. neerl.* **53**, 608.
Watts, C. A. H., Watts, B. M. (1952) Psychiatry in General Practice. London.

the technically inoperable from the biologically so, and must base surgery, not on anatomy alone, but also on the natural history of the disease. Surgery in the inoperable patient therefore is based on a different concept and has to be used in concert with radiotherapy, chemotherapy, and hormone treatment. Nitrogen mustard has proved of value in Hodgkin's disease, 6-mercaptopurine and aminopterine in other reticuloses, and actinomycin in rhabdomyosarcoma and Wilms's tumour. Hormonal treatment is of especial significance since this is the first attempt to alter the internal environment of a growth, rather than excise, burn, or otherwise destroy it; its mode of action is obscure since poison and antidote are the same. Indeed the use of œstrogens or androgens may make a particular patient with carcinoma of the breast worse, and this can be regarded as a clinical test of the hormone dependence of the growth and an indication for hypophysectomy or adrenalectomy. In Sweden, where all cancer is registered, 80% of cases cannot be controlled or cured by a surgical operation alone. In England and Wales 80,000 die each year from cancer, and for every 1 that dies 3 remain alive with growth. Sir Stanford Cade spoke of the improved chances of survival when radiation is added to orchidectomy for seminoma, of the complete relief of the distressing symptoms due to mediastinal obstruction when the neoplasm is irradiated with X rays, of the improved efficiency and less damaging effects of supervoltage X rays from a linear accelerator, and of the higher dosage now possible with radioactive cobalt. Though condemning the crime of operating on the inoperable, he considered that pelvic evisceration is indicated in advanced carcinoma of the cervix, since only thus can a patient be relieved of the appalling symptoms arising from fistulation, and of pain. Inoperable no longer meant hopeless.

Dr. DOUGLAS FRENCH spoke of the care of the cancer patient in general practice. He sees 20–25 new cases each year; 0·4% of his patients have cancer. The general practitioner is concerned with the beginning and the end of the disease. Diagnosis is sometimes delayed through fear or ignorance on the part of the patient, who may not wish to disclose a swelling for fear that it may be cancer, or may believe that rectal bleeding only indicates piles, or vaginal bleeding the menses. Delay occurs when the site of the growth is not obvious to the patient and the lesion is clinically silent. A patient who constantly visits the surgery with trivial symptoms is his own worst enemy since symptoms signifying a neoplasm then tend to be overlooked. He did not think that cancer education would have altered the outcome in the 23 patients he has seen this year, by bringing them any earlier to him. A negative report from a specialist should be regarded with the same reserve as a negative report on sputum examined for tubercle bacilli; it indicates that a lesion has not been found—not that none is there. In ten years he has seen 12 patients in whom the diagnosis was not established at the first hospital investigation; in 1 the lesion was in the brain, in another in the larynx, and in 10 in the alimentary tract. When the diagnosis is made, should the patient be told? If the outlook is good he may be, but when operation is impossible much depends on the mentality and intelligence of the patient and his desire, or otherwise, to live. Patients pass through three phases—optimism, doubt, and resignment. The moment to tell the truth is when optimism becomes doubt. Optimism and quiet of mind can be enhanced by giving dexamphetamine or amylobarbitone, and the patient should return to work. He has found deep X-ray therapy lowering, partly because the patient considers that the lesion has not been removed, whereas even a palliative operation leaves the impression that the growth has been taken away and often the symptoms due to metastases are not related by the patient to the original lesion. In the terminal stages pains develop anywhere and must be given names such as neuritis and rheumatism, and each a different drug, so that the changes have to be rung between the many proprietary forms of codeine and its mixtures, pethidine, aspirin with amylobarbitone, chlorpromazine, and morphine. For severe pain Dr. French gives the Brompton mixture containing morphine, heroin, and cocaine.

### Other Business

After the symposium Sir JOHN STOPFORD, F.R.S., vice-chancellor of Manchester University, was admitted to honorary fellowship of the college. The annual general meeting then ensued, under the chairmanship of Sir HARRY PLATT, the president.

## HOMOSEXUALITY

A SPECIAL committee appointed by the council of the British Medical Association has prepared a memorandum of evidence for submission to the Departmental Committee on Homosexuality and Prostitution. The following are among the committee's conclusions:

The apparent increase in homosexual practices and in prostitution is attributable to weakening of the sense of personal responsibility with regard to social and national welfare in a significant proportion of the population.

It is illogical that homosexual practices receive greater condemnation than promiscuous heterosexual intercourse.

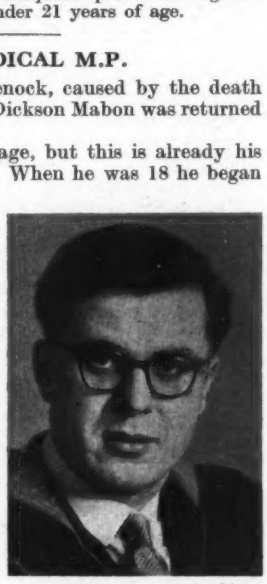
With regard to imprisonment for homosexual offences the committee suggests: (1) that prison is not usually the most suitable place for the punishment, deterrence, and reformation of the homosexual offender; (2) that if homosexual persons are sent to prison their segregation is neither practicable nor desirable; and (3) that if homosexuals are sent to prison, efforts should be made to ensure that the period of detention is effective and that they are deprived of opportunities for homosexual activity.

Legislation should aim at preventing seduction and reducing homosexual activities which are an offence to public order. If the law were relaxed with the result that homosexual practices between consenting adults were no longer an offence, (*a*) the age of consent should be not less than 21 years, and (*b*) the law should provide adequate protection against seduction by adults of those under 21 years of age.

## A NEW MEDICAL M.P.

AT the by-election at Greenock, caused by the death of Mr. Hector McNeil, Dr. J. Dickson Mabon was returned as a Labour member.

Dr. Mabon is 30 years of age, but this is already his third Parliamentary contest. When he was 18 he began work in the coalmines, and after 18 months he was released to serve in the Army. With an ex-Service bursary he began his medical studies at Glasgow University. As a student he was chairman of Glasgow University Labour Club and the National Association of Labour Students, and president of the University Union. He was one of the team of two who won the *Observer's* Students' debating competition last year, and he has led many student delegations to conferences abroad. He graduated M.B. last year. He has held a house-appointment at a Glasgow hospital, and spent a year in general practice. At present he is working in the public health and social medicine department of Glasgow University.



[Annan

# Public Health

## THE PUBLIC HEALTH IN 1954

### Chief Medical Officer's Report

IN the introduction to his report,[1] published last week, Sir John Charles, chief medical officer of the Ministry of Health, refers to a year featuring full employment, industrial prosperity, better food, and frightful weather: some readers may recognise 1954. The public health suffered no sharp shocks last year; but parts of the public conscience should feel distinctly uncomfortable when the report speaks about the increases in food-poisoning and dysentery.

#### VITAL STATISTICS

Sir John notes the steady fall in the infant-mortality rate, which at 25·4 last year reached its lowest level yet. The neonatal death rate—deaths in the first month of life—remained steady, while deaths from tuberculosis fell to the new low level of 178 per million population. The casualties of prematurity were the "outstanding subject" requiring investigation in the field of maternity and child welfare. Of 45,118 premature babies born in 1954 there were 3773 who did not live more than 24 hours. Losses on that scale in practically any other field would, Sir John feels, cause public concern.

There was another rise in cancer deaths, including lung cancer, despite the hope of the previous year that the upward trend had been halted. There was evidence that though the cancer mortality among males above the age of 55 continued to increase, the rates at ages below 55 had become relatively stable. There were 16,331 deaths in 1954 from cancer of the lung—a rise of 1199—and of these 13,995 were males.

#### FOOD-POISONING

The number of food-poisoning incidents in 1954 was 14% more than in 1953. Sporadic cases increased by 12%, family outbreaks by 49%, and general outbreaks by 3%. Whatever preventive measures have so far been taken have been ineffective, the report says. Once again the principal source of infection was the made-up meat dish, which is dangerous because of the time which elapses between preparation and consumption. Among the organisms responsible for 250 outbreaks were salmonellæ (13%), staphylococci (31%), and clostridia (15%). Assuming that salmonellæ needed safeguards which were not yet capable of large-scale application, the other two organisms mentioned were responsible for nearly half the outbreaks and in their case practicable precautions could be taken. Rapid cooling followed by proper refrigeration of meat dishes would almost eliminate food-poisoning due to clostridia. Similarly, prompt attention to minor injuries on the hands of food-handlers and the use of "no-touch" technique in the handling of cooked meat dishes would prevent staphylococcal food-poisoning. "It could be as simple as that!" Sir John remarks. The report lets the offenders down lightly when it says: "From the continued high incidence of food-poisoning, however, it was evident that certain caterers still found difficulty in applying these simple remedies."

#### FLUORIDATION OF WATER-SUPPLIES

During the year studies in readiness for the fluoridation of certain water-supplies were undertaken. The influence of small quantities of fluorine in the drinking-water upon dental decay in children and in adults brought up on such supplies was very striking.

In Slough, where the water naturally contains 0·9 parts of fluoride per million, 30% of a group of school-children between the ages of 11 and 16 living in the area since birth were completely free from dental decay: others, who were not born in the area but had lived there from the age of one or more, did not show such good results, only 12% being free from dental decay. It seems that fluoride exercises its greatest benefit on the teeth while they are in the stage of early development.

Referring to surveys which have already been carried out, Sir John says that one of the main objects was to attempt to correlate the degree of mottling of the teeth with the amount of fluoride present in the water. In the case of children born and reared at Slough, enamel opacities which would be noticed by the average intelligent parent occurred in not more than 1%; moreover, teeth were exceptionally well formed and there was remarkable freedom from decay.

#### NUTRITION

The report sounds a cautionary note. The freedom of choice now that rationing had ended, and the improvement of supplies, had led to an increase in the consumption of sugar and fats at the expense of protective and tissue-building foods. This change might not be of great significance to adults, but it might be harmful to children by displacing from their diet the constituents necessary for healthy growth. "This tendency seems to be particularly characteristic of family catering where the average protein intake expressed as a percentage of requirements is in an inverse ratio to the number of children. While accepting that we must not be too rigidly bound by theoretical standards of dietary sufficiency, it would be prudent to scrutinise closely the growth of children over the next few years for early indication of the effects of unbalanced nutrition so that timely measures may be taken to counteract it."

Referring to infant foods fortified by vitamin D, and the possibility of "virtual poisoning by vitamin D," the report says that an inquiry into the prevalence of this condition has been started.

#### SUDDEN DEATH IN INFANCY

Every year a number of babies are found dead unexpectedly in circumstances suggesting accidental suffocation. Death was usually recorded as from asphyxia, but increasing doubt has been thrown on this by findings both in the United States and in this country of evidence of pulmonary disease in some cases. To gain more exact information, the Public Health Laboratory Service agreed to coöperate in an inquiry with anatomists and social workers; and at Colindale, Cambridge, and Peterborough (and independently at the Hospital for Sick Children, Great Ormond Street) pathological and bacteriological examinations are now being made on babies dying suddenly without any obvious cause. The possibility of various infections, as well as of bacterial infections of the lung, is being borne in mind, but the investigation has not yet proceeded far enough to justify the drawing of any conclusions.

#### N.H.S. PRESCRIPTIONS

National Health Service statistics on prescribing show that in a sample of 127,809 prescriptions for drugs dispensed in the general-practitioner service in January, 1953, cough mixtures accounted for over 17% of the total, and medicaments for external use for another 11%. Laxatives and purgatives accounted for over 10%. "This is the range of homely remedies which used to be characteristic of the domestic medicine chest before the National Health Service came into being. There is no change of emphasis, but only of the providing pocket."

#### BLOOD-TRANSFUSION

The report refers to what appears to be an extravagant use of blood in modern hospital practice. It is suggested that much of the excessive use is due to a failure to appreciate the limitations of blood-transfusion and to lack of knowledge of the clearly defined indications for its use. The ratio of 24·5 bottles of blood issued for every bottle of dried plasma gave a pointer to a way in which a very considerable economy could be made. In certain conditions and circumstances dried plasma might satisfactorily replace whole blood and might even be preferable to it. Greater use of plasma would have the effect of making it more certain that patients who must have whole blood would not be deprived of it.

1. Report of the Ministry of Health for the year ended Dec. 31, 1954. Part II. On the State of the Public Health. H.M. Stationery Office. Pp. 252. 8s. 6d.

### STAFFING THE LABORATORIES

There are serious difficulties in getting suitable men to join the technical staffs of the hospital pathology service. Things are worse in some regions than in others; in highly industrialised regions, such as Manchester, the situation is particularly bad. A subcommittee appointed by the central pathology committee has been considering the problem. The report mentions some of its recommendations:

"Leaving aside the economic aspect of this problem, which is by far the most important one, there are some things which could be done to make the service more attractive to the youths selecting a career. The age entry for the first technical examination—the Intermediate Diploma of the I.M.L.T.—could be reduced from 20 to 19 years and it should be made possible for the bright boy to qualify sooner than his less gifted colleague. The apprenticeship of the student should be spent in a laboratory or group of laboratories giving a wide range of technical experience, and exploitation of the trainee by using him as a 'pair of hands' for dull repetitive low-grade work should be stopped."

### INFECTIOUS DISEASES

*Tuberculosis*

In the past six years mortality from tuberculosis has fallen by 64%, but the decline in the number of notifications of respiratory tuberculosis has not been nearly so great. Notifications in 1954 were only 14% less than the 1949 total. Better results are seen in non-respiratory tuberculosis, notifications of which fell by more than 50% between 1942 and 1954. The number of contacts examined continued to increase, though the number of new cases so diagnosed was now only about 2%. The waiting-list for institutional treatment fell by over a half in the past twelve months, the report records, and the situation should continue to improve until there will be no delay in providing accommodation at once for all patients who need it.

*Smallpox*

England and Wales had no case of smallpox in 1954, but Sir John again expresses concern at the low vaccination-rate among infants. For adequate protection at least 75% of infants should be vaccinated and a revaccination rate of about the same figure is desirable. In the year ending June 30, 1954, the infant-vaccination "acceptance rate" was 34·5% for the whole of England and Wales; the corresponding figure for 1953 was 34·2%. Acceptance-rates vary widely in different parts of the country: among the 49 English counties the 1954 rate varied from 5·8% in Derbyshire to 63·5% in East Sussex, and among the 79 English county boroughs from 1·9% in Leicester to 66% in Canterbury.

*Diphtheria*

In 1954, for the first time on record, the number of deaths from diphtheria reached a single figure. There were no deaths in children who had been immunised within five years of contracting the disease. Diphtheria is now less prevalent in the age-group 10–24 than it was in 1949, suggesting that effective immunisation is now better than it was at these ages. Estimates of the proportion of children under 5 who are now protected against diphtheria are as follows: under 1 37%, 1–2 56%, 2–3 64%, 3–4 70%, and 4–5 63%. These figures, the report says, are a tribute to the attention given by local health authorities to diphtheria prevention; but it seems that still higher percentages must be attained if the amount of the disease is to be reduced or, better still, eliminated in the younger age-groups.

*Dysentery*

In contrast to typhoid fever, which had virtually ceased to be a public-health problem in this country, dysentery took another "huge bound" in 1954, and at 31,858 notified cases was over $1^1/_2$ times higher than in 1953 and the highest on record. Fortunately, it was not very severe, and the ratio of deaths to notifications (0·1%) was the lowest yet recorded. Nearly three-quarters of the notifications related to children under the age of 15, and of this group those of 4 and under were twice as liable to the disease as their elders. There was evidence that the infection was largely transmitted directly from person to person and not by contaminated food. "Avoidance of spread involves cleanliness of body and clothing and, above all, thorough washing of the hands after each visit to the toilet."

## NOR ANY DROP TO DRINK?

IF one of the larger atomic weapons were exploded in a populated area, the survivors would have three main needs—shelter, food, and water. As a protection against the fall-out of radioactive products of an explosion, a roof would be the vital necessity; and a start has been made in assessing the available cover—not only houses but churches, barns, and byres—from Cornwall to Caithness. As regards food, large and dispersed stocks are promised, and many people are devoting long hours to training in the tasks of feeding a homeless multitude. But has the same attention, we wonder, been paid to the supply of drinking-water free from radioactive contamination? No part of these islands would be "safe"; and after even one single explosion all the exposed water over an area of perhaps a thousand square miles might receive lethal doses of radioactive dust. Some of this is soluble; and, though it may be detected, its removal from the water on any large scale is probably not feasible.

How much water would be required after such a catastrophe? The population, we may assume, will be scattered, partly by design and partly in panic, and in any rural area it may be greatly above the normal. For everybody life will be as hard as that of a soldier in the field, or harder; but one can hardly hope that weary and frightened civilians of all ages will display all the military virtues. The soldier has often existed on half a gallon a day; but, taking into account the dehydration of radiation sickness, 4 gallons seem a more reasonable figure for the civilian need.

The only water likely to escape radioactive contamination from the air is that which comes from wells and covered springs. In areas where most public supplies are drawn from deep wells, the demand should be satisfied so long as pumps and pipes escape damage. But many towns and villages, and almost all our large cities, derive their water from rivers or lakes or from gathering-grounds in the hills. To devise any protection for these is beyond human wit, and alternative supplies are essential. Small amounts of water can be moved by tanker vehicles, but the problem is too large for that solution. We must be prepared, therefore, to use every source, however small, which will yield water safe to drink. Almost all over the country there are small supplies, public and private, whose waters are not exposed. Many farms have sources sufficient for themselves, their cottages, and livestock. Old houses, both in town and country, almost always have wells: some are in use but some have been forgotten since a main supply was provided. Many ancient towns have disused springs which watered the citizens until a hundred years ago. The railways and industry own many large supplies unknown to outsiders. Whether all these would suffice to supply people's needs after an atomic explosion we cannot tell, but we believe that an important part of the preparations against such a disaster is that every supply in every district should be sought out, inspected, and catalogued. In many country districts much of this information is already in the hands of the sanitary authority, but much remains to be done. Upon the location of a relatively safe water-supply should depend all the plans for succouring the victims of atomic warfare.

Many of these smaller water-supplies do not reach the accepted levels of bacterial purity; but if one were faced with a choice of evils the rose spots of enteric fever would seem no more than cosmetic defects compared with the effects of internal beta radiation. Besides, the Army School of Hygiene has long experience of rendering the most dubious waters safe to drink, by methods which are neither expensive nor exacting in time or intelligence. Similarly the school should make available its knowledge of how to dispose of excreta in the field. In all the talk of Civil Defence we do not remember hearing this problem mentioned.

## Smog in the North-West

A report by the medical officer of health for Manchester, Dr. C. Metcalfe Brown, says that the climatic conditions during last month's severe fog [1] were similar to those responsible for the London fog in 1952—namely, an anticyclone with practically no wind, a lower temperature and higher humidity than usual, and a cold layer of air overlaid by a warmer layer. The fog developed on Nov. 16 and became more dense on the next two days. Thereafter it cleared, recurring in some districts from time to time, though not so densely until the end of November. The number of deaths on Nov. 18 was about $1^1/_2$–2 times the daily average for Manchester in November. A high proportion of the additional deaths were due to bronchitis. In Liverpool, on the other hand, it is reported that during the three foggy weeks there were fewer deaths than during the same period last year.

In Salford, Dr. J. L. Burn, medical officer of health, reported that several hourly readings on Nov. 17 and 18 revealed a higher concentration of smoke and sulphur dioxide than at any time during the London smog of 1952. During November, however, the total number of deaths registered in the city of Salford was 157, compared with 159 in November, 1954. Deaths from heart and respiratory diseases did, however, increase from 91 in 1954 to 99 in 1955. It is estimated that there were less than a dozen deaths in Salford which could be ascribed to the smog. On the other hand, morbidity was undoubtedly greater, and practitioners often had 20 extra calls to make daily. There were exacerbations of chronic bronchitis several days after the smog. Though there were few deaths, many patients with existing chronic respiratory disease became very ill. Asthmatics usually fared better than bronchitics. There was much tracheitis and minor respiratory infection, not all of which could be ascribed to the smog. The number of new claims for sickness benefit increased significantly. Judging from attendances at schools and nurseries, the staff were much more affected than the children. Many old people were able to stay in bed or in the house during the worst 48 hours. If the smog had lasted longer, many of them would have had to go out for shopping and so on, and they might have suffered much more.

## Report on Factories

In 1954 the number of people employed in factories increased to a new peace-time record. This increase is reflected in an increase of accidents—from 158,597 in 1953 to 161,458 in 1954 in factories only, and from 23,040 to 23,709 in other places covered by the Factories Acts. These figures are recorded by Sir George Barnett, chief inspector of factories, in his annual report.[2] The report shows that the accident-rate in 1954 was 22·4 per 1000 workers in factories, compared with 22·7 in 1953 and 22·5 in 1952. The accident-frequency rate (calculated from information provided by 2360 factories) was 1·62 per 100,000 man-hours, compared with 1·60 in 1953 and 1·61 in 1952. In 1954 there were 9522 accidents to boys and 3466 accidents to girls—increases on the 1953 figures of 288 and 117. Accidents to workers aged 60 or over numbered 13,552 in 1954, compared with 12,946 in 1953; but for the third year in succession the accident-rates for people aged 60 or over employed in factories were lower than the rates for those in the prime of life.

## Chiropody Service in London

At a meeting on Dec. 6 the London County Council adopted a recommendation of its health committee that the Minister of Health be asked to receive a deputation from the council to press for the development of the chiropody service provided by the council under the National Health Service Act. Previous deputations in April, 1952, and July, 1954, were unsuccessful, but the committee are impressed by the continuing and growing need for development of this service, which can do much to keep old people active and forestall trouble for the young. What the committee want is to provide 24 new foot clinics and 78 extra sessions to start with; these would give a service in those boroughs at present without it. 2 more clinics and 96 extra sessions would follow later, to fill gaps in the service elsewhere. The estimated cost is £10,370 in the first year and £5570 a year thereafter, rising to £11,100 ultimately.

1. See *Lancet*, Nov. 26, 1955, p. 1142.
2. Cmd. 9605. H.M. Stationery Office. 8*s*.

# Parliament

## QUESTION TIME

### Frontal Leucotomy Operations

Dr. DONALD JOHNSON asked the Minister of Health if he would state the number of operations for frontal leucotomy performed on involuntary patients in mental hospitals in England and Wales during 1952 and 1953; and, in view of the personality changes caused by such operations, what formalities were necessary for permission for such operations to be performed beyond the decision of the physician-superintendent of the hospital.—Mr. IAIN MACLEOD replied: Figures of leucotomy operations are not available for 1953, and those for previous years include voluntary as well as certified and temporary patients. In 1952 the number of operations performed was 1355. The decision to perform any operation on a mental patient under detention is one for the medical practitioner concerned having regard to his duty to preserve the patient's life and health. It is normal practice for the consent of the nearest relative to be obtained, if possible, and it is also customary for more than one doctor to be concerned in the decision as to this operation.

Dr. JOHNSON: Is the Minister aware of the warnings concerning the results of this operation issued recently by prominent specialists and research-workers in mental illness? Can the Minister ensure that wherever possible the consent of the patient is obtained for an operation like this, for even though certified and in involuntary detention he is in many cases a person enjoying free will and the powers of decision?—Mr. MACLEOD: I am well aware of those reports and of the anxieties which have perhaps given rise to this question. I am arranging—indeed we have already embarked on—a follow-up review within my department of cases of leucotomy.

Dr. EDITH SUMMERSKILL: Is it not a fact that in the Maudsley Hospital a board of doctors considers cases where frontal leucotomy is proposed? Would the Minister not advise other hospitals where possible to arrange for a number of doctors to consider these cases?—Mr. MACLEOD: I am not aware of the steps taken in the Maudsley Hospital in the consideration of these cases. We have regulations on these matters available on request to doctors, which have been drawn up by my Board of Control to meet these difficult circumstances. I should be glad to consider whether these rules—or advice is the better term—should be circulated to doctors.

Mr. J. B. HYND: Is the Minister aware of the very considerable concern caused by Press articles alleging that in an unnamed hospital in England experiments are being carried out for sheer experimental purposes on these patients? Can the Minister make any statement that will dispel that misgiving?—Mr. MACLEOD: I have seen these reports. In relation to the reference by certain papers to an experiment carried out by Dr. Sherwood, which was referred to in a paper before the Royal Society of Medicine, I am assured that the consent either of the patient or of relatives is always obtained in such cases.

### Diet of Old-age Pensioners

Replying to a question Mr. MACLEOD said that according to the National Food Survey the diet of old-age-pensioner households as a group, for the first half of 1955, in comparison with the scales of requirements adopted by the British Medical Association committee on nutrition, was adequate for all nutrients except perhaps iron where it was 92%. Except for vitamin C, where the difference was largely seasonal, the levels were all higher than in 1950.

### Nursing Courses for National Servicemen

Mr. STANLEY AWBERY asked the Minister of Labour if, in view of the shortage of male nurses for mental hospitals, steps would be taken to bring to the notice of young men due for call-up that if they wished to take nursing examination courses they could obtain deferment of National Service for this purpose and that there was a training allowance for each of the three years of training for them and their dependants.—Mr. HAROLD WATKINSON, parliamentary secretary to the Ministry, replied: I would like this to be as widely known as possible, and also the fact that the men who have trained as nurses will be able to continue nursing during their National Service. Special posters have been provided for exhibition at employment exchanges, particularly on days when men register for National Service, and leaflets giving full details about allowances during training are also available.

### Myxomatosis

Replying to a question, Mr. HEATHCOAT AMORY, Minister of Agriculture, said that, apart from small areas in the Midlands and the North, the whole of England and Wales had been largely denuded of wild rabbits as a result of myxomatosis. Examination of surviving rabbits suggested that the number that had acquired immunity was less than 1% of the former rabbit population.

### Heroin

In the House of Commons Mrs. LENA JEGER asked if the Home Secretary could say why, in view of the figures which had been published of the extent of heroin addiction in the United States, he imagined that the proposed ban would have any effect on addiction in this country.—Major LLOYD-GEORGE replied: I am simple enough to believe that, if large numbers of countries think that to ban heroin is a good thing to get rid of this appalling scourge, the contribution made by this country would help in some way towards it. The fact that the figures for the United States are as high as they are does not seem to me to be a reason why we should not join with other countries.

Sir ROBERT GRIMSTON: Will the Home Secretary make it clear, in any statement or white-paper that he issues, that this ban will not prevent the use of existing stocks of heroin? Will there not therefore be an intervening period when tests can be made and medical opinion crystallised? Will the Home Secretary give an undertaking that the Government will keep a close watch upon the matter, so that if the fears of a very large proportion of the medical profession prove to be right—and there is no proper alternative—the ban may be rescinded before the stocks of heroin have been exhausted?—Major LLOYD-GEORGE: Under the Dangerous Drugs Act the manufacture, import, and export of dangerous drugs can be carried out only by licence of the Secretary of State. This ban simply means that the manufacture, import, and export of heroin will cease, and that is all it means.

Replying to a further question Major LLOYD-GEORGE said that the quantity of heroin produced in this country in 1952 was 3104 oz.; in 1953, 3845 oz.; and in 1954, 4233 oz.

### Drug Traffic

Replying to a question Major LLOYD-GEORGE said that during 1954 there was 1 conviction under the Dangerous Drugs Act, 1951, for offering to supply drugs. There were 218 other convictions under the Act, the majority of which were for unlawful possession of drugs, but it was not possible to say in how many of these cases the drugs would have been sold to another person.

Mr. H. M. KING: Is the Minister aware that although the figures he has given show that the main ravages of the drug menace are outside this country, many of us are behind him and the Government in their linking up with other nations in a universal effort to stamp out this evil?—Major LLOYD-GEORGE: Whilst I have no evidence of any serious increase in illegal traffic in or use of drugs in this country there has been some increase in the traffic in Indian hemp, and I am watching this development closely.

Replying to a question asking what representations had been received from the World Health Organisation about the advisability of banning other drugs in addition to heroin, Major LLOYD-GEORGE said that the 18th session of the Economic and Social Council, which recommended the banning of heroin, also urged governments to prohibit the manufacture, import, and export of ketobemidone, and urged countries in which cannabis preparations were still being used to explore the possibility of discontinuing their use as rapidly as possible. Ketobemidone, which he was informed was an exceptionally addicting synthetic drug, had never been used in this country, and he did not propose to licence its import or manufacture here unless it was required for scientific purposes. Cannabis was used in small quantities as colouring matter in corn plasters and corn paints. He was informed that its use was on the wane. He did not propose to take any action at present to prevent its use.

### Poliomyelitis Vaccine

Replying to a question, Mr. MACLEOD said that no anti-virus-infection vaccine was being used in the National Health Service on contacts with cases of poliomyelitis, but some was being made of gamma-globulin derived from human-blood plasma.

## In England Now

*A Running Commentary by Peripatetic Correspondents*

IT'S a pretty hopeless task to keep up with the literature these days, but what one misses in the journals can often be picked up from unlikely sources. Last week the farming notes in our local rag reminded me that the Smithfield Show of 1952 provided one of the most significant clues for preventive medicine. The animals worst affected during the Great Smog were cattle housed under the most hygienic conditions, whereas the pigs and the sheep, which were not so assiduously toileted, escaped ill health. Apparently the ammonia produced neutralised the noxious acids in the air. I was sorry to miss making a relative ammonia-assessment at Earls Court this year, for we usually run up to Town in December to polish off the Christmas shopping, and alleviate any feeling of homesickness by slipping into the show to see who is winning the Angus *v.* Shorthorn battle. But I was there in 1952, and Earls Court was certainly pretty fruity. In fact we located the entrance by airborne scent through the gloom in spite of our own nasal congestion.

The cattle were tethered with only a southern aspect for the visitors, so that sentimental television-viewers would not block the telephone lines with offers of adoption, and so jeopardise the nation's meat-supply. Consequently the natural modesty of the herdsmen led them to rush around with pails and brooms. Sheep and pigs were much more discreet, and anyway most spectators had become hardened to Nature by the time they reached that section of the show. The ammonia-content of the air withered the medicated packing of our pocket nasal inhaler. The cilia on our turbinates lashed themselves into ecstasy. Our sinuses were supercharged with the precious vapour. We staggered back through the smog, drawing life from ethmoidal $NH_3$ till we reached Euston. By Bletchley the litmus was just turning. We were saved.

The moral is clear. Back to the middensteads! Those damned reformers never know where to draw the line. Who ever heard of smog deaths in Ireland? The little gintleman does more than pay the rent; he's far more efficient than all your fancy smog masks, and who likes eating fried smog masks anyway? Back to the days of Gardy Loo, and open up the River Fleet. What we lose one way we shall gain another. I don't say we should go as far as the monastic cult of self-induced ketosis, but the odour of sanctity kept away more than the Devil if our agricultural correspondent is right.

* * *

The other day I went to the R.S.M. to consult a classical work on *Tumours of the Breast*. This great book of some thousand pages was the fruit, as its distinguished authors, one English and one American, say in the preface, of thirty-five years' intensive study. The catalogue number was 618.19.006, but the shelf was empty. I asked one of the assistants to help me. In the fullness of time she located it—in the basement store. And the date of this sometime Last Word on the Matter?—1931.

* * *

Eskilstuna is often called the Sheffield of Sweden, and admittedly it is a centre of the steel industry, renowned for its cutlery and silverware. But there the resemblance ends. It has a population of about 60,000 people and is a clean, pleasant place, charmingly situated on the banks of the River Hjelmar. It has many houses of character, good shops and hotels, and attractive open spaces by the waterside. But the hospital has to be seen to be believed. Though it is a typical Swedish country hospital, its furnishings and equipment are enough to make any British provincial consultant's mouth water. Gaily decorated waiting-rooms with comfortable easy-chairs, occasional tables, and glossy magazines, are provided for outpatients. Attractive modern paintings are on the walls everywhere—in the X-ray rooms, and in "our little heart station, which is now after five years rather old." And the gardens are nearly perfect, with fountains playing among smooth lawns surrounded by masses of flowers. Flowers indeed are everywhere in Sweden; hardly a house is without them, and the window-boxes in every flat are ablaze with colour.

As I walked through this scene of delight towards the main entrance of the hospital I was unexpectedly accosted by a young man in white trousers and tunic. His perfect English was not unusual in Scandinavia; but fixing his eye on my tie, he greeted me as a fellow graduate. There are, it seems, too few doctors in Sweden, particularly in some specialties, and when a post as anæsthetist was advertised in the English journals my compatriot applied for the post. He has married a Swedish wife and loves the country of his adoption.

* * *

It was with some excitement that I saw in *The Times* a photograph over the caption "The Queen looking at a horse undergoing an X-ray and cardiograph test after opening the University's new veterinary school at Cambridge yesterday." In the interests of veterinary science it is much to be hoped that there are also available, as controls, records of the X-ray and cardiograph tests done on the horse before he carried out this, for him, doubtless novel and possibly somewhat arduous ceremony.

* * *

Our Greek patient did not understand much English, and conversation with her was limited. In an awkward pause I asked her what she understood by "Enosis." "Enosis?" she said in all innocence, "they are fruit salts."

* * *

I had been warned about the strain to which my alimentary canal would be subjected in Moscow. One authority advised the preliminary ingestion of blotting-paper; and although I did not accept this procedure literally, I had pondered the possibility of an appropriate substitute in the form of some modern pharmacological preparation.

So when I was led to the long table of what I supposed to be the appetisers, I restricted myself to a slice of smoked salmon and a saltspoonful of caviare: not because I like the stuff, but because it seemed a pity to neglect the opportunity. With self-complacency and condescending smile I stood back and watched the young athletes as they fell, like vultures or ravening wolves on the hard-boiled eggs, the cold meats, the fishes, and other less definable comestibles. Ha ha, my dear boys and girls, thought I, Nemesis awaits you. How will you fare later: what space will you have left when you are called upon to toss down glass after glass of fiery Vodka, and, since you may not offend your hosts by refusal, anaconda-like, attempt to dispose of a long succession of dishes? But with the passage of time a growing suspicion developed into certainty when dispersal of the assembled was obvious in its implication. I flew back to the trestle board but there was left not so much as would have sustained a tiny sparrow.

And so I repaired to bed nibbling chocolate with which I had provided myself before leaving England. Here at least I had shown some sense, for a bar of chocolate costs 18 roubles or about 32*s*. 6*d*.

* * *

The Minister of Health's appeals for economy in the National Health Service are making an impression—at least on the general public.

Examiner (showing an Esmarch's bandage): "Do you know what this is?"
First-aid candidate: "A rubber bandage."
"Quite right, what is it used for?"
"To stop bleeding in limbs."
"Yes, how long would you leave it on?"
"I don't know."
"Well, would you leave it on a week?"
"Oh no."
"Why not?"
"The rubber would perish."

* * *

*News from school.*—Science this term did not exist until one week ago when the first class was held. In accordance with this there is nothing much to be said. The top form did not make fireworks with Mr. J—— as they had hoped last term, and they also did not manage to make a thermometer, since the mercury had not come at the time. But still they have been going on with their experiments some of which are successful, and others not.

# Letters to the Editor

## HEALTH CENTRE OR GROUP PRACTICE?

SIR,—We have read with great interest the description of the Harlow health centres (Oct. 22)—a most impressive demonstration of health-centre organisation and medical coöperation. For us, however, this splendid example of good general practice is "too expensive." We are writing to show that such expenditure is not necessary for good general practice and health-service coöperation. There is real danger that such a magnificent and elaborate set-up may discourage practitioners from setting up "good general practice" on a less ambitious scale. To encourage them, we wish to make a few points which we have learned during the growth and organisation of our own practice, a group partnership of six in a semi-industrial suburban practice, within a new housing area.

Among the "unique features" of the Harlow centres, there are some which we consider undesirable, and others not unique. Efficiency and great economy is claimed. In our experience it is possible to achieve a design at least as efficient and certainly less expensive.

(1) The consulting-room need not be as large as at Harlow. In suites where there are two or more consulting-rooms, an examination-room can be shared by more than one consulting-room, and thus reduce the cost of building. (The cost of an examination-room is calculated at £180.)

(2) The consulting-room with examination-room, can be used for many purposes—antenatal clinic, baby clinic, conferences—which again reduces building cost.

(3) A specimen-testing room is a luxury. Any flat-bottomed sink installed either in the nurse's room, lavatory, or consulting-room will solve this problem. A sluice-room again seems unnecessary to "wash soiled mackintoshes and kidney dishes"; these can easily be dealt with in this sink. This saves a further room. Fewer rooms in the building means less walking and cleaning, and reduces both running costs and capital outlay. The introduction of such highly specialised rooms into general-practice planning, however desirable in hospital outpatient departments, seems uneconomic and really unnecessary.

(4) Local regulations may not permit a shelter for prams in front of a dwelling-house; the most that can be hoped for is a suitable space. But hundreds of child-welfare centres have worked for years without a covered-in pram-space. This is a desirable luxury, unobtainable in most areas.

(5) Record-keeping for any practice with three-quarters full lists or more takes more than a receptionist-secretary if it is not to take an undue share of the practitioner's time, particularly where there are morning, afternoon, and evening surgeries six days a week.

(6) Record-keeping of the National Health Service records in any new housing area is quite easily under-estimated. The amount of coming and going among the residents is quite remarkable. We find that a vast amount of time of our three secretaries is spent on these administrative efforts. It might be of interest that 86 ft. of shelves are needed to store the N.H.S. records of our patients.

(7) Coöperation with local authorities does not depend on buildings. It depends on the willingness to coöperate by both sides. Health visitors, tuberculosis health visitors, district nurses, and district midwives are frequent, regular, and welcome colleagues in our practice.

(8) To have the dentist in the same building is by no means essential to good relations.

(9) Electricity as a means of heating is a mistake, as we have found. The additional capital cost of an automatic gas or oil controlled central heating might well have been more practicable and cost-saving than the pram shelter.

(10) What has been described as unique and a special problem at Harlow holds good all over the country, wherever there are new housing estates, with their high rents, few shops and other facilities, increased distances from work and school, and the wide-open door to the high-powered hire-purchase salesman. Though Dr. Stephen Taylor and his colleagues describe their capital expenditure as modest, the sums involved seem hopelessly unrealistic; and our experience demonstrates that much less than £1 per patient is possible as capital expenditure for a general-practice unit, if the work

is so organised that the maximum use is made of all available space. In our experience the capital expenditure on buildings and all accessories was 13*s.* 3*d.* per patient. This includes the capital cost of adapting two neighbouring buildings and purchasing one, and building and furnishing a third premises completely, to include multiple consulting-rooms with examination-rooms, waiting-rooms, and record space, and space for the all-important member of our team, the nurse.

(11) In employing two full-time nurses at the surgeries, we find they make a fundamental contribution to good general practice, particularly in a new housing area where these nurses run a minor outpatient department.

(12) Industrial health is also part of our practice; in our area there are five major industrial undertakings, of which two are visited regularly by two of us, whilst two others have other general practitioners attending and advising them. One of the factory ambulance-rooms is linked with our automatic internal telephone system, which serves all our premises and rooms.

In conclusion, we would like to make it clear that our discussion of the Harlow health centres is not meant in any way to detract from their value, but we hope that other general practitioners may realise what can be done without large capital sums.

C. E. MUNRO
E. V. KUENSSBERG
A. R. LAURENCE
G. MACNAUGHTAN
A. H. D. LARGE
G. IRVINE.

Edinburgh.

## SLUICE-ROOMS

SIR,—In a number of hospitals that I have visited recently I have noticed what I consider to be a dirty and dangerous practice—dangerous particularly in children's hospitals. Fouled mackintoshes, urine bottles, and other infected vessels are washed out in the sluice-room in a sink which is also used for cleaning and filling patients' wash-bowls. It may well be that the contamination of the wash-bowls in this way is small, but it is certainly an unpleasant practice. Another sink should be provided somewhere (not necessarily in the sluice-room) where bowls can be washed, filled for serving, and stored nearby.

It would be a good thing if doctors would take notice of the processes that go on in sluice-rooms and not ignore the doubtful hygienic practices in some of them. It may be found that the nurses' techniques are unsound, but it is more than likely that faults would be attributable to lack of space, inadequate equipment, and insufficient interest on the doctor's part in applied bacteriology for the *whole* of his department.

London, W.1. HUGH GAINSBOROUGH.

## POSITIVE OR NEGATIVE ?

SIR,—From time to time discussion arises about the reproduction of radiographs for publication. Is it better to have a positive print (in which the radio-opaque areas, such as bones and barium-filled stomach are black) or a negative print which looks the same as the original film ? I favour the positive print. At each stage in the transition from what is visible to the radiologist to what the reader sees in the textbook or journal, there is inevitably some loss of definition; but the last stage (positive to negative print) is avoidable and should not, I think, be used. Moreover, it costs twice as much to reproduce a radiograph when this extra processing is involved.

It is hard to see what advantages there are in presenting radiographs as negative prints. The chief advantage of a negative is its translucency, and this is lost when it is reproduced on paper. For viewing the original films, transmitted light is used, and the luminosity of the transparent areas is so great that they stand out as solid objects. No reproduction can give this brilliance and solidity. For the same reason, a picture of a stained-glass window never has the life of the original. But the positive radiograph gives a sense of solid bones and solid radio-opaque material in the viscera that the negative never can.

Radiologists are accustomed to both sorts of picture; but for the ordinary reader it would surely be better to have a uniform method of reproduction which gives the clearest result—namely, a positive print. Moreover, such a print accords with the accepted photographic rule—a negative to look *through* and a positive to look *at*.

London, S.W.16. A. P. BERTWISTLE.

## ECLAMPSIA

SIR,—Dr. Salzmann (Nov. 5) states that a diet rich in first-class protein may prevent toxæmia of pregnancy, while carbohydrates undermine the resistance of the expectant mother to invasion by fœtal hormones, either male or female.

It is true that Hamlin,[1] after he began putting his patients on a diet, found that eclampsia had disappeared from his clinic. But Hamlin is still, in his own words, observing many cases of mild toxæmia.

In 1938 a countryman of Hamlin, Dr. Arthur Wilson of Melbourne, spoke on eclampsia in Amsterdam, at the International Congress of Obstetrics and Gynæcology. In Melbourne from 1910 to 1937 severe eclampsia was very common. In Dr. Wilson's opinion this high frequency might be associated with the high meat consumption in Australia—the highest in the world, according to the League of Nations (annual consumption 107·2 kg. per head, compared with 62 kg. in England and 42·5 kg. in Holland).

In 1950 Hamlin stated that in Sydney eclampsia was still a much-feared complication of pregnancy; whereas this disease is unknown in the Javanese population of nearby Indonesia, as many Dutch observers have remarked.

I note that Hamlin's diet includes much meat and two pints of milk daily, but only three ounces of bread.[2]

The diet of the population of Holland during the war was quite different: some kind of whole-wheat bread, potatoes, vegetables, cereals, a little meat, 250 *g.* butter once weekly, and far less dairy products than people here are used to. Expectant mothers also received some milk-powder. During this period eclampsia became very rare and mild toxæmia disappeared; and this was the experience in most European countries. During the last months of the war many had to live under conditions of semi-starvation; and when the people received more food eclampsia again became common.

The opposite observation has been made in sheep by Parry,[3] who induced toxæmia of pregnancy by feeding these animals large quantities of hay and green fodder and putting them thereafter on a starvation diet (chiefly mangolds). Toxæmia of pregnancy in sheep is very similar to that in man, although there are clinical differences. In toxæmia of sheep the adrenal-cortex/thyroid ratio is doubled, probably through enlargement of the adrenal cortex, which in starvation becomes hyperplastic.[4]

It seems to me worth while to try for pregnant women a diet somewhat resembling that in Holland during the war, with more bread, vegetables, cereals, potatoes, far less meat and fat, and no dairy products at all; McCance and Widdowson [5] have described their experiences with such a diet, without meat, in an orphanage, and on the whole these have been favourable. (The Javanese eat no dairy products, but cover their need of fat with coccs-oil; and whereas toxæmia is unknown among them, it occurs among Europeans in Indonesia, who mostly eat European food.)

1. Hamlin, R. H. J. *Lancet*, 1952, i, 64.
2. Hamlin, R. H. J. *Proc. R. Soc. Med.* 1953, **46**, 393.
3. Parry, H. B. *J. Physiol.* 1954, **126**, 40P. Parry, H. B., Taylor, W. H. *Ibid*, 1955, **127**, 54P.
4. Hottinger, A., Gsell, O., Uhlinger, E. Hungerkrankheit. Basle, 1948.
5. McCance, R. A., Widdowson, E. M. *Lancet*, July 30, 1955, p. 205.

Dr. Salzmann's suggestion that fœtal gonadal hormones are responsible for the appearance of œdema in pregnancy reminds me of the work of Taylor et al.[6] who were of the opinion that œstrone, progesterone, and testosterone, circulating in the mother's blood, caused retention of sodium; but this was before it was known that cortical adrenal hormones, such as aldosterone, are strong mineralocorticoids. To me it seems that fœtal hormones can only augment the quantity of the circulating maternal hormones, from which they are not different in any respect. An allergic reaction is in my opinion improbable.

Amsterdam. R. SCHUURMANS.

## STAFFING LABORATORIES

SIR,—We are very much in agreement with Mr. Snow and his colleagues, whose letter appeared last week. The proposed grading of laboratory technologists is most undesirable.

Under these proposals many senior and experienced men will not be eligible for the higher scales of pay, since remuneration is to be related, not to the skill and experience of the technologist concerned, but to the numbers of staff employed in the laboratory or division.

This particularly concerns the histology section, where it must be rare for a staff of four to be employed in any but the largest laboratories, whereas in bacteriology it is almost the rule to have at least this many.

The effect will be felt most in the smaller laboratories, where it is essential to have good senior men; present staff may well leave for better-paid posts in larger laboratories and future applicants be wanting.

More realistic salary-scales are needed in the present senior grades, possibly with an extra allowance for special responsibility, but without introducing new categories among the grades.

County Hospital, Hereford. W. H. J. BAKER
D. R. CHRISTIE.

## AN INTRACTABLE FOLEY CATHETER

SIR,—Like your peripatetic correspondent (Nov. 5) I was recently faced with the problem of a Foley catheter the bulb of which could not be deflated by opening the side-tube or aspiration through it.

The patient was referred from another hospital where the catheter had been inserted to relieve an attack of acute urinary retention. A cystoscopic examination was planned to decide on the best type of prostatic surgery, when this technical hitch was encountered.

After a workmanlike pull on the catheter had failed to produce the desired effect, a cystoscope was passed into the bladder alongside the catheter. An attempt was made to cut the bulb with a pair of cystoscopic scissors, but the rubber proved too tough. The cystoscopic biopsy forceps could not be made to grasp the tense bulb. Both the coagulating and cutting diathermy was next tried with the result anticipated by your correspondent.

The catheter was labelled "5 cc." (indicating the capacity of the bulb), and it was decided to further inflate the bulb to try and burst it. Finally fully 140 c.cm. was injected; but, except for the appearance of suprapubic swelling, nothing happened. No doubt the bladder wall protected the bulb to some extent.

Suprapubic exploration was being seriously considered. A cystoscope was passed again, as a final effort, and advanced quite vigorously after it had engaged the prostatic urethra. A dull "pop" was heard, the suprapubic tumour disappeared, and the catheter floated out. Unfortunately, with the explosion the bulb had come off completely and was still in the bladder. It took a few more minutes to catch this evasive bit of rubber, floating in the air-bubble, with a biopsy forceps.

On one or two previous occasions I have found with this type of catheter that, although fluid or air can be injected into the bulb, it will not deflate; possibly the communicating channel is very small in parts or acquires a valve-like defect during the manufacturing process. A preliminary test of these bulbs would appear to be a good routine—to test not only the integrity of the bulb but also whether it will deflate normally. If a 5 c.cm. bulb holds up to 140 c.cm. a liberal safety margin can be assumed.

Edendale Non-European Hospital, Pietermaritzburg, Natal, South Africa. THEUNIS COETZEE.

6. Taylor, H. C. jun., Warner, R. C., Welsh, C. A. *Amer. J. Obstet. Gynec.* 1943, **45**, 547.

## IN THE MENTAL HOSPITAL

SIR,—There is one common factor underlying the complaints of recent writers on this topic. It is the strange twilight state of being poised unhappily between the old "asylum" and the at times astonishingly artificial world of the modern mental hospital.

One of the difficulties with the "lunacy reformer" as referred to by Dr. Yellowlees (Dec. 3) is his energetic and sometimes thoughtless drive away from the old abuses straight through to the new ones. It is axiomatic that our big problem has always been and still is the chronic psychotic. Psychiatrists appear to be in danger of spontaneous subdivision into what may be termed "psychotic psychiatrists" and "neurotic psychiatrists"—according to predominant interest. There is often something approaching fear and distrust between the "psychotics" and "neurotics" on a hospital staff. A preference for the psychotic patient and the standard range of physical treatments often goes with the urge to change everything and create the new artificial world of the mental hospital, which threatens to outdo the old asylum in rendering people permanently unfit for the normal rigours and frustrations of any natural society.

Perhaps Dr. Bickford's picture (Dec. 3) of the older psychiatrists hardened and brutalised by "daily acquaintance with dreadful things" is exaggerated. It is surprising the amount of turmoil the young enthusiast can create in a mental hospital before he recognises his common human limitations and his specific personal ones. Surely psychiatry is one discipline where experience, maturity, and wisdom count for something?

The status of occupational therapy nowadays appears to vary in direct proportion to its lack of practical usefulness.

In line with current artificiality, the more remote the occupation from the kind of things that would occupy and interest the patient in the real world outside, the better. Hobbies and handcrafts of various kinds have their place, but should not—as is the tendency in some quarters—completely replace more vigorous and muscular activities that improve appetite and sleep and reduce the need for nocturnal sedation. Opposition comes from many quarters because such activity may be called "work" rather than occupation and be associated with the patient helping to keep his current house and garden in order. The opponents of such useful activities have different reasons for their opposition and usually make uneasy bedfellows.

This abuse of occupation to the minimising or exclusion of useful activities is another example of the chronic "over-correction"—possible exploitation of patients in the past now tending towards an unconsidered and emotional ban on all domestic, agricultural, and horticultural activities. There seems no good reason for ensuring that the patient's activities in hospital are as remote as possible from his or her normal interests and work in the real world outside the hospital.

This aspect of the great artificiality applies more particularly to the younger, short-stay, and newly admitted patient. Too often he gladly falls in with the new philosophy and so prolongs his unfitness for the necessities of the real world; and in being so encouraged is often contributing to his readmission or series of readmissions.

I agree with Dr. Martin (Dec. 3) that the doctor is inclined to hide behind his white coat and all that it implies. One of the better modern trends is the improve-

ment in interpersonal relations between nursing staff and doctors. This could be further promoted by the doctor hanging up his white coat more often and mixing with his patients and nursing staff on more or less equal terms. Something on these lines was referred to by Dr. Maxwell Jones in a recent talk on his approach to those most difficult people called psychopaths. It is part of the laudable tendency to approach the whole problem of mental illness in terms of socialised and socialising groups, with medical and nursing staff as integral parts of those groups. I find that the "neurotic psychiatrist" (of my terminology above) is more inclined to develop along these lines than the "psychotic psychiatrist," who tends to cling to his white coat, his air of scientific mysticism, and his impersonal dealings with patients almost exclusively through the media of his physical therapeutic agents. Useful and essential as they are, they are but a part of treatment and possibly by no means the greater part.

If, as Dr. Martin points out, the nursing staff should be far more au fait with the intricacies of interpersonal relations, how much more the doctor? Perhaps for both too much stress is laid on physical psychiatry in training, and the inevitable and permanent human factor is apt to be mislaid—sometimes along with common sense and the maintenance of a firm, conscious appreciation of the issues and values of the real world outside the increasingly artificial milieu of the mental hospital.

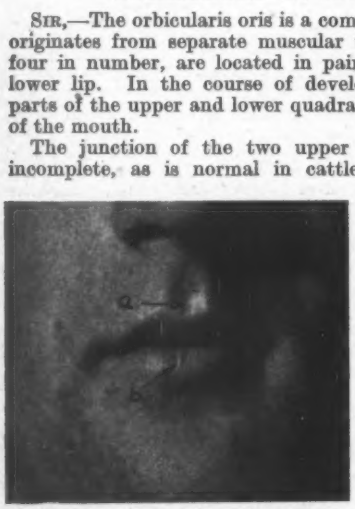
After the beneficent reforms that have come about we should be on guard against the "lunacy reformer" with his strange and fatal tendency to substitute new abuses for old. The chief danger is the creation of an artificial environment within the mental hospital that threatens to resemble some appalling synthetic society of the future as imagined by our more pessimistic novelists—thus retarding rather than accelerating the patient's return to a real world outside the gates of the hospital.

Coton Hill Hospital,
Stafford. H. M. FLANAGAN.

## COMMISSURE IN LOWER LIP

SIR,—The orbicularis oris is a compound muscle which originates from separate muscular units. These units, four in number, are located in pairs in the upper and lower lip. In the course of development the median parts of the upper and lower quadrants join in the angle of the mouth.

The junction of the two upper quadrants may be incomplete, as is normal in cattle, or complete but complicated by the formation of the philtrum, a shallow groove in the upper lip, as it is in man.




*a*, philtrum; *b*, commissure between two lower quadrants of orbicularis oris.

The lower lip is smooth and its morphological deviations are usually expressed in the formation of the groove or even a sulcus in the middle part of the lip. In rare cases the junction of two lower quadrants may be marked by the development of a distinct commissure. The persistence of the commissure between the lower quadrants of orbicularis oris in the adult male is shown in the accompanying figure. A commissure is regularly shaped and extended through the whole width of the lower lip. According to the information obtainable, two other members of the same family, both females, have a similar shape of the lower lip.

Thus the persistence of the commissure between the lower quadrants of orbicularis oris may be an expression of hereditary genetic constitution, and could be used in observations related to the human constitution and human genetics.

Department of Anatomy and Parasitology,
University of Queensland, Brisbane. R. TUCKER.

## NEW SHORT-ACTING THIO-BARBITURATE

SIR,—I was much interested in the letter by Dr. Shegog Ruddell in your issue of Nov. 26. A few months ago a clinical trial of sodium 5-allyl-5-isobutylthiobarbiturate (thialbutone sodium) was undertaken at Chase Farm Hospital and I set out [1] the results of a small series, to which Dr. Ruddell refers. These confirmed the claims of the German workers Weese and Koss [2] and Dietman [3] regarding the rapid recovery of consciousness and striking absence of postoperative drowsiness and confusion. Since then a further series of 43 patients has been studied, allowing a more critical assessment of the drug.

The preparation used in this series was supplied by May & Baker Ltd. under the non-proprietary name of thialbutone sodium.

The patients' ages ranged from 13 to 80. They were divided into two groups according to whether premedication with an opiate was given or not.

*Group 1* included 18 patients; 14 had no premedication and 4 had atropine (gr. $^1/_{100}$) only. 11 of them were outpatients and the operations included orthopædic manipulations, incision of abscesses, and reduction of simple fractures. The dose of thialbutone ranged from 0·25 g. to 1·4 g., supplemented in some cases by nitrous oxide. A few patients were also given succinylcholine.

*Group 2* included 25 inpatients premedicated with an opiate and atropine or scopolamine. The operations were mostly herniorraphies and varicose-vein ligations; there were 2 hysterectomies and a partial gastrectomy. Supplementary nitrous oxide/oxygen and relaxants were used as required. Total dosage of thialbutone varied from 0·45 g. to 2·4 g., given mostly as intermittent injections following an induction dose of 0·5 g. In 3 cases the induction dose was followed by continuous intravenous infusion of the drug as 0·6% solution in normal saline.

Duration of unconsciousness was judged by the time taken to register complete awareness of surroundings in response to questioning. The duration of postoperative drowsiness, blood-pressure readings, and the time taken by the patient to sit or walk unaided were noted as far as possible.

*Side-effects*

Several side-effects and sequelæ were noted which had not been evident in the original small series. The number in each group was as follows:

| | *Group 1* | *Group 2* |
|---|---|---|
| Nausea and vomiting | 2 | 4 |
| Drowsiness lasting 1 hour after operation | 5 | 18 |
| Drowsiness lasting more than 6 hours | 0 | 3 |
| Hiccough | 5 | 3 |
| Clonus and trismus | 2 | 3 |
| Marked fall in blood-pressure | 0 | 3 |
| Postoperative headache | 1 | 2 |
| Retrograde amnesia | 0 | 4 |

Postoperative drowsiness was not usually severe but it was much commoner when the patient had had premedication.

In 2 cases in group 2 where the drug was given by the "drip" method a severe fall in blood-pressure followed induction. These patients had 1·7 g. and 1·58 g. respectively, and each showed postoperative somnolence for about 24 hours. It is noteworthy that 5 unpremedicated outpatients were still drowsy and unable to look after themselves at the end of an hour, though each had less than 1·0 g. This contrasted with the other 13 unpremedicated patients, who awoke within a few minutes of induction, had little or no residual drowsiness, and were fit to return home within $^1/_2$ hour.

Hypotension was severe in 3 normotensive middle-aged females. 2 had intravenous thialbutone before hysterectomy,

1. Nobes, P. *Lancet*, 1955, 1, 797.
2. Weese, H., Koss, F. H. *Dtsch. med. Wschr.* 1954, 79, 601.
3. Dietman, K. *Chirurg.* 1954, 25, 185.

and had total doses of 1·58 g. and 1·7 g. respectively. The 3rd had only 1·0 g. before dilatation and curettage.

This drug is much superior to either of the thiobarbiturates, thiopentone and thialbarbitone ('Kemithal'), as regards rapid recovery of consciousness. Weight for weight, it is less potent than either, and a dose of at least 0·5 g. is necessary to maintain adequate anæsthesia in outpatients, even during operations lasting only 10 minutes.

Delayed recovery, however, is a drawback and therefore the drug cannot, I think, be unreservedly recommended for routine use, even in carefully prepared outpatients. On the other hand, if thialbutone sodium is used purely for induction in such cases and if full use is made of supplementary nitrous-oxide/oxygen maintenance, then a smooth and rapid recovery can be predicted far more confidently than with other intravenous agents used in the same way.

Turning to some of the points in Dr. Ruddell's letter, I never noted wretching in any patient during induction, but a few patients vomited during the recovery phase; all but one had had opiate premedication. In the unpremedicated adult, if the maximum dose is confined to 1·0 g., then 4½–5 minutes is perhaps an unnecessarily long time for giving the dose.

My thanks are due to Dr. P. W. S. Gray and Dr. D. Zuch for their help and encouragement. Messrs. Bayer of Leverkusen kindly supplied their drug ('Baytenal') used in the first series, and I am grateful to May & Baker. Ltd. for the thialbutone sodium ("Transithal") used in the second series.

London, N.10. PETER NOBES.

## HYDROCORTISONE IN PAINFUL SHOULDER

SIR,—I have read with interest the correspondence arising from the article by Mr. Murnaghan and Mr. McIntosh (Oct. 15).

I had been using procaine 1% in these cases for some time; but when hydrocortisone appeared on the market I changed to this. For a long time now I have been of the opinion that the results were not significantly different. I have found that if the patient has not benefited from the injection of local anæsthetic he is unlikely to derive relief from the introduction of hydrocortisone at the same site. The most important point seems to be to deposit the solution at the "correct site." The addition of hyaluronidase to the solution of local anæsthetic does not seem to lessen the importance of this.

Morse, Saskatchewan, Canada. M. GLASSMAN.

## CHEST PHYSICIANS

SIR,—In their letter of Nov. 5 Dr. Hendry and Dr. Tattersall spoke of the grading committees' harsh treatment of some former members of the tuberculosis service. There is no doubt that gross injustices were done to senior physicians in charge of chest clinics (of whom I am one) at the time of the inception of the National Health Service and since, in that few of them were raised to consultant status although their long experience in this special branch of clinical medicine entitled them to be so elevated; and there is equally no doubt that the regional hospital boards, the selection committees, and the Ministry of Health remain quite unconcerned at the plight of so many skilled and experienced physicians.

The Royal Colleges of Physicians and Surgeons have established such a stranglehold upon the profession that virtually nobody can hope to be appointed to a consultant post unless he holds the membership or fellowship; and I believe that in ninety-nine cases out of a hundred the colleges direct the policy of the regions and the selection committees.

The medical profession in this country is bedevilled with a variety of registrable and unregistrable diplomas such as exist I believe in no other country in the world, and I am not aware that we are the better doctors for them: a man is known by the quality of his work, not by the diploma he holds.

NON HABET.

## A REPORT FROM HOSPITAL

SIR,—I note from Mr. Gruber's letter (Dec. 3) that in trying to achieve brevity I have fallen into obscurity.

I should perhaps have made it clear that when I wrote to the surgeon asking for information about one of his patients he replied giving me precisely the information I wanted but asked me to write to the administrative chief of the hospital for an official report. The report I eventually had from the house-surgeon via the administrator was equally courteous but in no way more informative than the letter I had already had from the senior surgeon.

I entirely agree with Mr. Gruber that consultants are almost always glad to inform and advise about their patients, and the present consultant was no exception. The administrative merry-go-round in this case was, however, new to me.

London, N.1. R. E. W. FISHER.

## PROTOPHRENIA

SIR,—Dr. Bourne's article of Dec. 3 brings to the notice of all who work in the psychiatric field with children a very important problem which I think many of us have been aware of for years. This statistical study, coming from an institution dealing with young grossly mentally deficient children, pinpoints the importance of nurture in achieving full potential development. Nevertheless I think Dr. Bourne does less than justice to the problem of vulnerability. He points the analogy with the tubercle bacillus, whose pathogenicity none would question "though the vast majority infected with it are not ill." This does not in any way answer the question why some are and others are not; and in making a similar study of family case-histories, some of them pursued over years, it has seemed to me that the very striking absence of affected siblings does suggest that the piling up of difficulties, plus some unknown source of vulnerability to such difficulties, may be sufficient to turn what could have been a normal development into a severely distorted one.

It has been my custom to regard most of these children as psychotic, prefacing any remarks I may make about them with a clear statement that in this context we hardly know what psychotic means. Dr. Bourne regards it as a condition which may be treatable if taken in the early stages, and quotes the therapeutic work of Rank in Boston. Even with intensive psychotherapy, however, many such children do not come back to a wholly normal course of development, and some have to be regarded as permanently "atypical," and ultimately are often lost sight of as members of the mentally defective population. Perhaps the most important point that he makes is the real need, in building up ego function, that adjustments and associations should be made at the stage of development to which they normally belong. However successful therapy is in retracing the steps and in re-forming sounder relationships, a good deal of evidence is accumulating that it is only rarely possible for these children to make a full return to normal.

Reverting to Dr. Bourne's rejection of the term "psychotic," surely a child makes some kind of ego organisation at however primitive a level from the time that he begins his separate existence? Disintegration occurring at a very early age prevents many further integrations from taking place, and I would have thought the concept of ego disintegration was valid, provided we are able to establish at least some very early normal function. It is characteristic of some of these histories that they include abnormal maternal attitudes which are

emotionally damaging, although not based on the gross, almost perverse, deviations referred to by Dr. Bourne. Nevertheless, we need to remember that these children, with their aloofness and inability to respond, almost could be said to exact from their parents a corresponding quality of aloofness in order to come to any sort of terms with the child's peculiar way of functioning.

Department of Psychological Medicine,
The Hospital for Sick Children,
Great Ormond Street,
London, W.C.1. E. M. CREAK.

SIR,—It is most stimulating to find that there are people like Dr. Bourne who are not content to leave the poor mental defectives in statu quo, even though I am not sure that I can agree with all he says.

I am not certain to which group his article refers; for if one removes the "organics" from institutional defectives one is left with the so-called "primary aments" and also the "psychotics." This latter group comprises the children who show psychiatric symptoms over and above mental defect. If the very small group of Dr. Bourne's "residuals" refers to the latter, I hope that it will promote renewed investigations in child psychiatry and also in mental hygiene. If the small group refers to the "primary aments" I feel that some of the conclusions are wide of the mark; for in my experience of some seven years with defective children these "primary aments" are not only mental dwarfs but also in many cases physically dwarfed without there being any definite organic lesion to account for it. Here we find this group a most interesting group for study, and we hope one day to be able to replace the term "primary ament" with some more exact diagnosis; for this term at its best is a confession of ignorance and at its worst tends to be a bar to further investigation, since it suggests that nothing can be done.

Our impression here is that the whole organism is striving to develop in the face of some disorder of the *milieu intérieur*. Modern research shows that this is not such a wild idea as at first it seems to be. One has only to think of the errors of carbohydrate metabolism such as sucrosuria and galactosuria to realise that irregular metabolism of some simple factor in the diet can completely upset the "works." Error of metabolism of one amino-acid such as occurs in phenylpyruvic amentia can have very far-reaching effects, as is well known. These are but two of the simpler types of metabolic disorder that spring to mind.

If one postulates that the cause of some cases of "primary amentia" is metabolic, then one is faced with a problem like searching for the proverbial needle in the haystack. However, the needle seems to me to be there, and we hope to continue our search amongst a few blades of straw in spite of Dr. Bourne's findings.

Botleys Park Hospital,
Chertsey, Surrey. GORDON DUTTON.

## RESISTANT TUBERCLE BACILLI

SIR,—Further to the letter of Dr. Murdoch and Dr. Grant in your issue of Oct. 8, we can now report on tests carried out to ascertain whether the isoniazid-resistant organisms from the case which these workers reported earlier (Sept. 17) were *Mycobacterium tuberculosis*.

Following the suggestion of Dr. Mitchison and Dr. Selkon (Sept. 24) we have tested for cord formation, catalase production, growth at room-temperature, and Mantoux conversion in guineapigs. The culture from this patient showed cord formation, was weakly catalase-positive, and did not grow on agar medium or egg-glycerin medium at room-temperature. Two guineapigs, which were Mantoux-negative before inoculation with the culture, both had an area of induration 14 mm. in diameter when tested with 1/100 Old Tuberculin five weeks later.

All of these tests give variable results both with true tubercle bacilli and with saprophytic organisms, but we feel that the consistency of the results with this strain, together with the supporting clinical evidence, leave little doubt that the case is one of pulmonary tuberculosis due to an isoniazid-resistant strain of *M. tuberculosis*.

Department of Tuberculosis,
University of Edinburgh. SHEILA M. STEWART
A. T. WALLACE.

## THE RING AND THE SWOLLEN FINGER

SIR,—Removal of a ring from a swollen finger after injection of hyaluronidase, which Dr. Ryder describes (Nov. 26), has been previously reported by Birch.[1] In an annotation last year [2] you referred to the reduction of paraphimosis by means of local injection of hyaluronidase.

London, S.W.10. F. ERNEST WEALE.

## ADRENAL HÆMORRHAGE

SIR,—Your annotation of Oct. 22 prompts me to report the following case of suprarenal hæmorrhage.

The patient, who, when he died earlier this year, was 53 years old, had had a long and varied history of ill health. In 1943 he was in hospital for investigation of chronic œdema of the legs. The cause was found to be low plasma-protein, due to jejuno-ileal insufficiency resulting from old tuberculous peritonitis. In 1946 visual difficulty due to a pituitary tumour developed. At craniotomy a chromophobe adenoma of the pituitary was removed. In February, 1955, he was admitted to hospital on account of colicky abdominal pain, nausea, and recent constipation.

*On examination* the patient was pale and ill, with wheezing respirations and massive œdema of the legs and lower abdomen. There was some generalised abdominal tenderness. Temperature 97°F; pulse-rate 64 per min.; respirations 24 per min.

*Treatment and course.*—Intestinal obstruction was tentatively diagnosed, but the patient was treated conservatively owing to his poor general condition. During the next two days his condition changed little. On the third day he was taking solid food but was still complaining of abdominal pain, and his pulse-rate had risen to 80–100 per min. Late in the afternoon of that day he suddenly became unconscious, had convulsions, and frothed at the mouth. The pulse became weak and the pupils pin-point, and he died.

*Necropsy.*—There was severe œdema of the legs, with hyperkeratosis of the skin. The lungs were œdematous and congested, and both pleural sacs contained much clear straw-coloured effusion. The peritoneal cavity was a mass of widespread dense fibrous adhesions, involving principally the jejunum and ileum. There was no evidence of intestinal obstruction. The mesentery contained some hard fibrous areas. Both suprarenal glands were enlarged and firm. On section the medulla was distended with recent blood-clot, the cortex forming a thin outer boundary to the areas of hæmorrhage. The pituitary was replaced by soft yellow-grey tissue, filling an enlarged pituitary fossa and extending upwards around the optic chiasma.

*Microscopic examination.*—The pituitary tumour was a chromophobe adenoma. In the suprarenals the medulla was distended by recent hæmorrhage, and the cortex included widespread areas of necrosis. There were occasional groups of polymorphs beneath the capsule. Some extracapsular veins were occluded by thrombus, showing no evidence of organisation. No organisms were demonstrable by staining, and there was no evidence of tuberculosis. The appearance suggested that the hæmorrhage was secondary to thrombosis of the suprarenal veins, but no changes were present in their walls. The mesenteric lymph-node examined showed great increase in fibrous tissue between the follicles.

This case illustrates a rare, fatal condition. If diagnosed in life, it should be treated by administration of noradrenaline.[3]

Thanks are due to Dr. C. Pike, consultant morbid anatomist, and to Mr. T. G. E. Loosemore, consultant surgeon at the Peace Memorial Hospital, for permission to publish this case, and for their help and advice.

Peace Memorial Hospital,
Watford, Herts. O. P. GALPIN.

1. Birch, C. A. *Brit. med. J.* 1954, ii, 595.
2. *Lancet*, 1954, ii, 180.
3. Millard, A. H. *Postgrad. med. J.* 1954, **30**, 495.

## CONSULTANTS IN DERMATOLOGY

SIR,—Venereologists in general fully endorse the protest made by Dr. Ingram (Nov. 26) against the reuniting of the specialties of dermatology and venereology.

In the pre-arsenical era, syphilis undoubtedly presented as a skin manifestation in many instances. The changing characteristics of the disease in the past twenty years now throw emphasis more especially on the cardiovascular and nervous systems.

At the beginning of the late war the Army system of "dermatologists" who practised both skin and venereal diseases still existed, and many eminent men from both specialties were enlisted in the dual capacity. The divergence of the two groups of diseases was soon appreciated and the necessity for consultants in each distinct branch accepted, from War Office level downwards.

During the war, and since, the teaching of potential consultants for each specialty has continued to remain apart and there are no young trainees qualified to practise both adequately.

Dermatology and venereology each has its own problems, and dermatologists are quite untrained to cope with the epidemiological aspect of venereal disease, the modern clinical manifestations of syphilis, and the greatest problem of venereology today—non-specific urethritis with its peculiar complications—any more than the venereologist is trained to cope with the complex aspect of modern dermatology.

The "V.D." scheme so well established in our country provides the highest standard of treatment and confidence for our patients. The dual appointments now contemplated by the administrators can only destroy the effectiveness of the V.D. system and must surely prove detrimental to dermatology as well.

Sheffield. DOUGLAS J. CAMPBELL.

SIR,—It must be recognised that while in certain minor centres of population the constant presence of a venereologist might be amply rewarded by the prevention of the maladies with which he is concerned, there would scarcely be enough skin disease to sustain the interest of a fully trained dermatologist—who would know only too well that efficient and progressive dermatology requires a large, active, and well-equipped clinic.

In a substantial proportion of cases a skin disease is not merely a local disorder reversible by the application of lotion or ointment but a symptom of profound bodily illness, often emotional; and it may be said on behalf of the patient that if he cannot be sent to such a centre where he can be listened to, thoroughly and definitively investigated, or admitted forthwith as an inpatient should he happen to need it, it is probably better for his health that he should not see a specialist at all. Yet more than half the patients attending hospitals for skin trouble in the North-west are disposed of at the rate of 20–30 attendances per hour by a consultant working alone: indeed in one region the *average* number on which it was proposed that sessions should be based was 19·5.!

It cannot be denied that patients and their family doctors seem to be perfectly satisfied with this sort of thing; moreover, those who take seriously their designation as consultants and who prefer to use the traditional method of history-taking, thorough examination, and explanation are given fewer sessions and are held in less esteem by the authorities, who, relying on the twin popular beliefs that skin diseases are produced by dust, liquids, and vapour and are to be cured by ringing the changes on lotion, ointment, and wigs, naturally regard the matter in terms of "production."

If the dispensary technique demanded by the public (and its medical advisers of first instance) is truly the best for its health, then it is clear that these trained and highly qualified young men should, for the sake of their own happiness, seek some other use for their capabilities. If, however, it is considered that the patient is entitled, whether he demands it or not, to a thoughtful consideration of his case then there is plenty of work for them as consultants in certain big centres to which they can perhaps no longer be attracted as registrars.

Manchester. J. H. TWISTON DAVIES.

## HEROIN

SIR,—As the Minister seems to be using the annotation and special article in your issue of Dec. 3 as justification for his attitude towards the ban on heroin, it is only right that you should be criticised for this.

In my opinion, you are guilty of special pleading of the worst order, and I am shocked that what I have always considered to be a leading scientific journal in medicine should stoop to such an unscientific method of presentation of the case. My fear is that similar such arguments will be used in the future when, for *some political reason*, any drug (such as pethidine) may be banned for medical use in this country.

Let us face the issues fairly and squarely:

(1) You admit (although only in brackets) that this step is "something never done before," that it is "important," but, in spite of the fact that the whole of the British Medical Association is clearly against the ban, you state that this idea of democracy is limited to those who think in terms of majorities and mandates. Later on in your annotation you state that "on pure principle, no answer is possible to the argument that heroin must not be banned so long as there is a single doctor in Britain who wants to use it."

Surely, Sir, you must be suffering from schizophrenia? You cannot, as the editor of a responsible medical journal, whose opinion is quoted in the House of Commons, go on from the above statements to say that we should keep the ban because if 10% of our fellow citizens become heroin addicts (something which is medically absurd) a practitioner might no longer be allowed to prescribe heroin. Medicine would soon be in a sorry state if the right of doctors to prescribe what they thought fit were given up. *This ban is bad. It is wrong.* I treat heroin addicts. I also treat alcoholics. On your arguments I should petition for a ban on alcohol. I must point out that, so far as addiction is concerned, alcoholics are a far greater menace to public life than heroin addicts. Such a pussy-footed argument regarding a ban on alcohol would be derided by the august columns of your journal.

(2) We all know that the banning of heroin production will make addicts ten times worse. The Americans have proved it. My own addicts are assured by peddlers that they will be able to obtain their supplies of heroin after Dec. 31 (at a price). Ipso facto, banning is the wrong method of stopping heroin addiction. Have we, as doctors, got to suppport the wrong method of tackling a medical problem because the Home Secretary and the Minister of Health are in a political jam?

American doctors are petitioning for the removal of the ban in America. Why should we not support them instead of W.H.O.?

(3) To turn to the article "Doing Without Heroin" I could also pick a lot of unconnected statements (out of context) from medical books and journals and make a case for the use, or abuse, of any drug in any disease if my time were not limited by treating patients. For example, Hillis[1] pointed out that codeine is of no value *whatsoever* in cough. The Science Committee of the B.M.A. and the Council, as recently as 1954, stated unequivocally that heroin was indispensable. A matter of opinion? Maybe, but where does that get your article?

To return to your annotation: I understood that it was the British Medical Association who was protesting against the ban and said so at its Council meeting on Nov. 4. Backed up by the Fellowship for Freedom in Medicine on the following day. Can you honestly maintain, in view of this, that you agree with the banning

1. Hillis, B. R. *Lancet*, 1952, i, 1230.

or rationing of drugs to doctors for medical purposes on any grounds?

Finally, do you really believe that the patient in pain who needs heroin and cannot manage on the "Lancet Cocktails" cares whether the human community ends on the Cliffs of Dover or not?

J. L. McCALLUM
Member of council, British Medical Association; assistant hon. secretary, Fellowship for Freedom in Medicine.
London, W.C.1

## THE RARITY OF FATTY LIVER IN AFRICAN BANTU ALCOHOLICS

SIR,—In the South African Bantu adult population there is a high prevalence of hepatic fibrosis and cirrhosis, yet "alcoholic cirrhosis," with the associated fatty change, is virtually absent. Thus, Dr. J. Higginson, of this institute, in several hundred necropsies and liver biopsies, has noted obvious fat deposition in the liver in 4 out of 55 patients with severe cirrhosis, but none at all in biopsy specimens of liver from 15 hard-drinking pellagrins. These findings confirm earlier observations by Gillman and Gillman [1] on the very low prevalence of fatty liver in Bantu adults.

Concerning the alcohol intake of these people, according to our calculations fermented cereal foodstuffs, which are consumed habitually in large volumes, may provide a mean daily intake of alcohol probably reaching or exceeding the mean intake of the drinking population of the United States—i.e., about 30 ml.[2] But quite apart from the consumption of these foodstuffs (which are slowly imbibed often throughout the day), in the large centres of population there is a tremendous consumption of illegal, highly intoxicating drinks by a somewhat restricted group of Bantu adults. A special branch of the police force is required to deal with this illicit liquor production.

Sinclair [3] states that evidence indicates that alcoholic cirrhosis is caused by a deficiency of lipotropic substances; that in the early stages fatty infiltration is completely reversible, but if not treated leads to fibrotic changes; further, that alcohol has no direct effect on liver cells in producing cirrhosis. From our knowledge of local food habits, we very much doubt whether the diet consumed by Bantu alcoholics is richer in lipotropic substances than that of similar Europeans—rather the reverse. Under conditions, therefore, when one would expect to find fatty liver to be common, this is not so. The question arises: is it possible that an *endogenous* lipotropic agent is involved, whose presence and activity are characteristic of the Bantu though not of Europeans?

Lansing,[4] of Washington University Medical School, fed rabbits with purina rabbit chow including 0·3 g. cholesterol per diem—a diet which produces fatty livers and aortic atheromatosis in almost all animals after six weeks' feeding. The treated animals received daily doses of pancreatic elastase simultaneously with the cholesterol; the controls received no elastase. The administration of elastase resulted in almost complete inhibition of fatty livers. After six weeks there was a clear reduction of prevalence and severity of atherosclerosis, which was not as complete as the effect on the fatty livers. The implication is that elastase, in addition to affecting elastic tissue, is lipotropic. Lansing considered that it was most unlikely that results were due to proteolytic liberation of methionine in the intestinal tract. By analogy, therefore, is it at all possible that pancreatic elastase plays a part in protecting Bantu alcoholics against the development of fatty liver?

Balo and Banga, of Budapest, have produced evidence suggesting that there is little elastase present in the pancreas of adults who die from coronary-artery disease, in contrast to the far larger amount in the same organs of those who die young or relatively free from atheromatous lesions.[5]

Turning back to the Bantu, Dr. Higginson and Dr. Pepler,[6] of this institute, have shown that from naked-eye assessment the severer complications of atherosclerosis in the Bantu are only about a tenth as common as among corresponding Europeans. In relation, specifically, to aortic lesions, we have almost completed analysing a large series of total aortæ from Bantu and European patients, from youth to old age. Results indicate that, speaking generally, in relation to fatty degeneration, the aortæ of even elderly Bantu do not become much "older" than those of young Europeans.

It therefore seems reasonable to expect to find a high level of elastase in the pancreas of Bantu adults. But one would expect to find a low level in the pancreas of children with kwashiorkor (among whom fatty liver and, incidentally, pancreatic lesions and dysfunction are almost characteristic), in contrast to a high level in healthy Bantu and European young children.

We would, of course, gladly put these speculations to the test; but unfortunately we cannot secure fresh pancreases within an hour or so of death, after which elastase activity rapidly decreases. We therefore hope that other research-workers dwelling among similar primitive peoples may be able to determine the pancreatic-elastase activity in the groups cited.

Should our speculations be valid, the unexpected rarity of fatty liver in Bantu alcoholics may be linked with the relatively low degree of fatty atheromatous lesions in the blood-vessels, and both phenomena may be associated with, or promoted by, a high level of pancreatic-elastase activity.

This letter is published with the permission of the South African Council for Scientific and Industrial Research.

Human Biochemistry Research Unit, South African Institute for Medical Research, Johannesburg, and South African Council for Scientific and Industrial Research.
ALEXANDER R. P. WALKER
MARIANNE ANDERSSON.

1. Gillman, J., Gillman, T. Perspectives in Human Malnutrition. New York, 1951; p. 242.
2. Jellinek, E. M. *Proc. Nutr. Soc.* 1955, **14**, 93.
3. Sinclair, H. M. *Ibid*, p. 107.
4. Lansing, A. Symposium on Atherosclerosis. Publication no. 338, National Research Council, Washington, 1954; p. 50.

## THE FORGOTTEN PATIENT

SIR,—Dr. Bickford stands, I think, in no great need of a champion; but you yourself might like perhaps to know that there is at least a minority movement which has looked at his articles with a different eye.

I, Sir, am responsible for what goes on in one of the mental hospitals of which Dr. Bickford writes; and, as on a previous occasion, we are circulating his provocative articles among our nursing staff. The initiative this time at least came from the Chief Male Nurse, who with me felt that they might well be used to strike sparks off any of us who are too well used to or satisfied with things as they are.

This is a hospital which I shall hope to show to Dr. Bickford some day, and I think that even at present we might escape classification among the worst three in the country; but to suggest that nothing of what he has to say could have relevance for us would be a pathetic admission of lack of insight. This word "insight," to which we are so devoted, is the touchstone. General hospitals or even orthopædic hospitals may know little of mental mechanisms; but who are we to reveal so obviously that Dr. Bickford flicks us on the raw?

As one of your respected correspondents reminds us, there have been lunacy reformers before. Before Lomax there was James Birch Sharpe and his select commission of 1815; and before him Pinel. Dr. Bickford will not expect immediate canonisation. But a man's reach should exceed his grasp, or what's a retirement pension waiting for?

Hellesdon Hospital, Norwich.
F. J. NAPIER
Medical Superintendent.

5. See *Brit. med. J.* July 2, 1955, p. 34.
6. Higginson, J., Pepler, W. J. *J. clin. Invest.* 1954, **33**, 1366.

## INSTITUTIONALISATION

SIR,—With reference to Dr. Martin's most pertinent article on Institutionalisation (Dec. 3), one basic remedy would be to break up the large mental hospital into smaller units, and to bear this in mind when planning future institutions. This seems self-evident to most who work in this field, but it is apparently less obvious to the planning authorities. The second most important aspect in this problem is that of medical and nursing traditional routine, which may need revision. Last but not least—and despite many changes—there is still sometimes a tendency to forget that the hospital administration exists to serve the patient and not vice versa.

Department of Psychology,
The Fountain Hospital,
London, S.W.17. LYDIA MUNDY.

SIR,—Is the introductionalisation of the word "institutionalisation" (Dec. 3, p. 1188) really essentialisational?

Newcastle upon Tyne. M. H. ARMSTRONG DAVISON.

*** Perhaps not. But can Dr. Armstrong Davison suggest any other single word, or even two or three words, with the same signification?—ED. L.

## CHOLERAGENIC AND NON-CHOLERAGENIC VIBRIOS

SIR,—It is common in the literature on cholera to find the terms "choleragenic" and "non-choleragenic" applied to vibrios, and sometimes they are given more meaning than they really deserve.

The division of vibrios into these two classes was a corollary to the definition of *Vibrio choleræ* by Gardner and Venkatraman.[1] The background to this work was the impossibility of deciding the pathogenicity of a vibrio by experimental means. A working hypothesis was needed for the ætiological agent of cholera and also a means of identifying it by a practical laboratory procedure, so as to simplify the application of public-health measures. Attention was therefore directed to identifying the vibrio associated with the majority of cases which the clinician's judgment led him to believe were true cholera and not severe diarrhœa.

The laboratory tests finally evolved by Gardner and Venkatraman had no rational connection with any possible pathogenesis, and were based on serological and hæmolytic properties, so combined as to distinguish the desired vibrio. Although this definition has served well as a working hypothesis, the problem of cholera remains serious, as the mortality figures show. It is also hard for epidemiologists to discover a reservoir of *V. choleræ* to which epidemics can be traced.[2] As a result, some epidemiologists[3] challenge the contention that *V. choleræ*, as defined by Gardner and Venkatraman, is the only class of vibrios known for certain to cause epidemic cholera. Because "non-agglutinating" vibrios alone could be isolated from some patients showing the clinical features of cholera, they maintain that, except for a preconceived notion about the exclusive character of *V. choleræ*, there was no reason for rejecting the "non-agglutinable" vibrio as causal agent.

One possible reason is implied by Taylor.[4] If all the vibrios, other than *V. choleræ*, which are found in rice-water stools are considered as causal agents, they form a great many serological groups, and the serologist feels that the cause of cholera must lie in one, or at most a few, serological groups. The epidemiologist, on the other hand, thinks that the vibrio undergoes quick serological changes, so that potentially all vibrios are dangerous. This is the view that my hypothesis[5–7] of cholera pathogenesis also leads to.

According to this hypothesis, certain extracellular hydrolases of all vibrios can act on the constituents of the intestines and blood-vessels, and can increase the permeability of these membranes. Diarrhœal organisms like *V. metchnikovi* and *Pseudomonas pyocyanea* also give rise to such enzymes.

The mortality due to diarrhœas in the recorded vital statistics of India is sometimes as high as that due to cholera. If we readjust our view of the ætiological agent of cholera, it is quite likely that some of the diarrhœal deaths may come over to the cholera columns.

The term "non-choleragenic" seems most unhappy when applied to the El Tor vibrios of Gardner and Venkatraman's O subgroup-I. To reject the enzyme hypothesis means reviving the old "endotoxic" view. If we believe in the chemical basis of the immunological reactions, the O substance of both *V. choleræ* and the El Tor vibrio (of this group) must be the same, or at least have much in common, and hence must contain the same endotoxin. What then is the mechanism by which the El Tor vibrio loses its pathogenicity?

Central Research Institute,
Kasauli, India. E. K. NARAYANAN.

## ANTISEPTIC LOZENGES

SIR,—As general practitioner and as bacteriologist, we have both been impressed by the possible value of the quaternary ammonium compound cetyl pyridinium chloride against bacterial infections of the throat or mouth. This substance, a cationic detergent freely soluble in water, has been used occasionally for many years for disinfection of skin and mucous membrane, but may, we believe, deserve more attention.

One of us (J. D. B.) has determined the germicidal activity of cetyl pyridinium chloride in vitro against recently isolated strains of *Streptococcus hæmolyticus*, *Staphylococcus aureus*, and *Bact. coli communis*.

The dilutions of cetyl pyridinium chloride were made with physiological saline; the tubes were kept at 37°C; and the time the organism was exposed to the action of the antiseptic was 10 minutes. At the end of that time 0·25 ml. of a 0·01% solution of sodium stearate was added to the tubes to inactivate the cetyl pyridinium chloride, and subcultures were made on blood-agar. The dilutions necessary to kill the test organisms in 10 minutes at 37°C with comparative tests under exactly similar conditions using phenol, were:

| | *Cetyl pyridinium chloride* | *Phenol* |
|---|---|---|
| *Strep. hæmolyticus* .. .. | 1 in 120,000 | 1 in 190 |
| *Staph. aureus* .. .. | 1 in 80,000 | 1 in 90 |
| *Bact. coli* .. .. .. | 1 in 50,000 | 1 in 120 |

In-vivo tests on throat lozenges containing cetyl pyridinium chloride* were made using the following technique:

The mouth and pharynx were washed with a quantity of sterile water for a standard time. The sterile water was expectorated into a sterile tube and a standard quantity withdrawn and spread on to blood-agar plates and incubated for 24 hours at 37°C. After this preliminary washing, the lozenge under test was allowed to dissolve in the mouth, after which the mouth and throat were again washed with a standard quantity of sterile water which was again expectorated and an identical amount of the expectorated fluid was withdrawn and spread over a second agar plate. This process was repeated for a succession of the lozenges under test.

Using this technique, the following kinds of lozenge were examined.

A. Formaldehyde *B.P.C.*
B. Penicillin *B.P.*
C. Tyrothricin, 1 mg.; benzocaine, 5 mg.
D. Domiphen bromide, 0·5 mg.
E. Chloroxylenol, 0·055%; benzylphenol, 0·014%; blackcurrant juice, 7·0%.
F. Bacitracin, 50 units, tyrothricin, 1 mg.; benzocaine, 5 mg.
G. Cetyl pyridinium chloride, 4 mg.; sodium propionate, 100 mg.; benzocaine 5 mg.

In order to avoid any carry-over of the active ingredient on to the culture plate the vessel into which the subject

1. Gardner, A. D., Venkatraman, K. V. *J. Hyg., Camb.* 1935, **35**, 262.
2. Seal, S. C. *Indian med. Gaz.* 1945, **80**, 414.
3. *World Hlth Org. Spec. Rep. Ser.* 1952, no. 52, p. 5.
4. Taylor, J. Cholera Research in India, 1934–40 (Indian Research Fund Association), Kanpur, India, 1941.
5. Narayanan, E. K. Biochemical Activities of *V. Choleræ* and Related Organisms. University of Madras, PH.D. Thesis, 1954.
6. Narayanan, E. K., Menon, P. S. *Nature, Lond.* 1952, **170**, 621.
7. Narayanan, E. K., Devi, P., Menon, P. S. *Indian J. med. Res.* 1953, **41**, 295.

* Manufactured under the name of 'Procidets' by Messrs. Harker Stagg.

expectorated contained in each case a suitable inhibiting agent—e.g., in the case of a penicillin lozenge penicillinase was used, and in the case of lozenges containing quaternary ammonium salts the inhibiting agent was sodium stearate.

With lozenges A to F, countless colonies were regularly grown from the fluid expectorated after dissolving four lozenges in the mouth. With lozenge G, on the other hand the counts were reduced by 55%, 75%, 83%, and 90% after using one, two, three, or four lozenges respectively. In tests on 50 people, four of these lozenges reduced the oral flora, on the average, by 90%. In a further series of tests on 6 persons with hæmolytic strains of streptococci in the mouth it was shown that these strains were killed by the first lozenge.

In general practice, trials of lozenge G, in about 200 cases of stomatitis, oral ulcers, tonsillitis, pharyngitis, and glossitis, have produced what seemed to be unusually beneficial results, the infection usually clearing within two days.

London, N.9. N. B. BENJAFIELD.

London, W.1. J. D. BENJAFIELD.

## AN INCOMPLETE VICTORY

SIR,—At this stage of the battle against tuberculosis empty beds do not mean victory: they mean that the unknown casualties have been left neglected on the battlefield by a health service which has failed to find them. The policy of the tuberculosis service should be "find and heal." These two objectives should have equal emphasis.

At present we are ignorant of the basic facts necessary to the design of a rational programme of tuberculosis control—namely, the prevalence of unknown cases in different areas and their distribution by age and sex. These facts should be found by a survey of a random sample of the population by the mass-radiography units.[1]

If we are to find the bulk of unknown infectors with our present poor resources the mass-radiography units must cease to offer an ideal personal-protection service to a few regular patrons and try to break new ground by examining people whose chests have never been radiographed before. To persuade the unexamined segments of the population to come forward for examination would probably require a campaign on a national scale. The health-service administration is unwilling to launch such publicity, for fear that the existing token mass-radiography service would be swamped. I believe that (apart from maid-of-all-work duties such as providing general practitioners with unlimited facilities, examining works contacts, and doing miscellaneous operational research jobs) the mass-radiography units should, with Government-aided publicity, make a supreme effort to examine as many as possible of the male population over 45 years of age who have never been examined radiographically. This would have a massive effect on the volume of free-floating tuberculous infection, because it would drain the unknown infector pool of most of its long-term members. The male over 45 should be our target for three important reasons: (1) this group has the highest prevalence of tuberculosis in those of its members who have not been examined radiographically; (2) these are the really long-duration infectors, many of whom could have been diagnosed twenty years ago; (3) this group has a low radiographic attack-rate—i.e., in comparatively few men over 45 will a new lesion develop after they have once been found to be radiographically clear. The clearance effect of examining this group (i.e., the persistence of effect of lowering the number of unknown infectors) will be maximal.

Mass X-ray Service for South West London, Grove Hospital, London, S.W.17. F. A. NASH, Medical director.

1. Nash, F. A. *N.A.P.T. Bull.* April, 1954.

## NITROGEN MUSTARD IN NERVOUS DISEASES

SIR,—In 1949 I recorded[1] some of my experiences with nitrogen mustard in the treatment of bone tuberculosis, and I should like to add some new facts from clinics in Poland and elsewhere confirming the anti-inflammatory and anti-allergic action of this substance.

Secco et al.[2] found that paralyses in children with tuberculous meningitis disappeared more quickly after streptomycin plus nitrogen mustard than after streptomycin alone. Similar observations were made in the Warsaw University clinic of children's diseases by Professor Michalowicz and his colleagues.

These properties of nitrogen mustard produced a dramatic response in paralyses caused by pressure of inflammatory exudate on nerve-trunks, as well as in vascular and trophic neural lesions. These findings were confirmed in a large series described by Klimkova-Deutschova,[3] from Professor Henner's clinic in Prague, and by the findings of Professor Jakimowicz, Horodyński, Jarema, Kiczak, and others in Poland.

With Professor Wilczek, of Krakow, I have observed particular benefit in some patients with the clinical picture of optic atrophy, which had resisted other treatment. It is true that we obtained positive results in only about 25% of cases, but the very fact that sensitivity to light returned, followed by marginal sight, in refractory cases is a therapeutic success. In a few cases of optic atrophy the results were very successful.

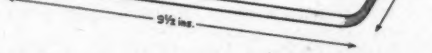
Our empirical observations have found an experimental basis. It was believed that nitrogen mustard acted as a "stressor" causing an increase in the blood-level of endogenous cortisone. The work of Romero[4] then showed that nitrogen mustard induced in the suprarenal cortex similar changes to corticotrophin. Recent reports[5] of the successful use of cortisone in strokes and other nervous disorders confirm our empirical observations.

Nitrogen mustard has been given in doses ten times smaller than usually used for tumours—namely, 0·5 mg. daily, repeated 5–10 times. A further 5–10 doses were given if necessary after an interval of three weeks.

III Internal Clinic, Medical Academy, Krakow, Poland. J. ALEKSANDROWICZ.

## PREVENTION OF BLEEDING DURING VEIN-STRIPPING

SIR,—When stripping the internal saphenous vein, it is well recognised that it is of the utmost importance that no hæmatomas should occur. For this reason most surgeons operate on the empty vein, in the high Trendelenburg position. Even so, immediately after the avulsion, hæmorrhage may occur in the thigh, and pressure for five minutes is all important. Usually the assistant supplies this with his hand, but even so there may be some bruising of the thigh. During the past few months, however, we have tried the effects of pressure applied by means of a plastic strip (see accompanying figure). Since using this method of compression the amount of bruising has been extremely slight.




Even though this instrument is so simple, by its proper use a troublesome complication can be avoided.

R. ROWDEN FOOTE
MARCUS FREDMAN.

London, W.1.

1. Aleksandrowicz, J. *Lancet*, 1949, i, 547.
2. Secco, C., Benini, S., Vittone, A. *Policlinico*, 1951, sez. prat. 58, 1537.
3. Klimkova-Deutschova, E. *Čas. Lék. čes.* 1950, 89, 572.
4. Romero, E. *Rev. clín. esp.* 1952, 47.
5. Russek, H. I., Russek, A. S., Zohman, B. L. *J. Amer. med. Ass.* 1955, 159, 102.

# Notes and News

## CLINICAL RESEARCH MADE EASIER

Now more than two years old, the Institute of Clinical Research at 40, Hanson Street, London, W.1, has been finely equipped for investigations by members of the senior staff of the Middlesex Hospital, and by juniors whose work they sponsor. As it could be a prototype for institutes at other teaching hospitals, its progress will be followed with attention; and the exhibition arranged on Dec. 6 was encouraging. Clearly, the opportunities for experimental observations on animals are valued highly by surgeons and others who do not readily find such facilities; and, under the administrative direction of Prof. Alan Kekwick, the institute is providing for more and more solid work by a greater variety of workers.

Subjects under study include the substitution of aorta or 'Orlon' tubes for œsophageal segments (Mr. D. H. Patey); bone growth and repair (Mr. Philip Wiles and Mr. K. Dawson); jejunal replacement of the common bile-duct (Mr. Vaughan Hudson and Mr. F. A. Henley); and the effect of cortisone in X-ray damage in cancer of the lung (Mr. Holmes Sellors and Dr. J. B. Walter). Professor Kekwick is studying, with Mr. G. Pawan, the effect of altering the proportions of carbohydrate, fat, and protein in isocaloric diets, and with Dr. R. de Mowbray the relation of dietary fat to serum lipids and lipoproteins. Dr. Evan Bedford and Dr. Short had some fine post-mortem radiographs displaying the blood-vessel appearances characteristic of various forms of pulmonary hypertension; Dr. Lawson Macdonald illustrated renal and vascular changes caused by hypotensive therapy; Dr. A. J. Hewer and Dr. P. Coles are investigating induced hypotension; Dr. D. H. P. Cope and Dr. D. E. Argent are examining the ætiology and treatment of cerebral anoxia; and Mr. L. P. Le Quesne and Dr. M. Hobsley use Evans-blue extraction for estimating blood-volume. Dr. B. A. Sellick showed apparatus for hypothermia, and Mr. R. Mowlem and Mr. D. Crockett are studying œdema fluids. The Middlesex Hospital's reputation in endocrinology was upheld by several exhibits of work by Sir Charles Dodds, F.R.S., Prof. J. E. Roberts, Dr. J. D. Nabarro, Dr. Oliver Garrod, Mrs. S. A. Simpson, Dr. J. F. Tait, Miss A. Moxham, Dr. G. Walker, and Mr. Pawan. Dr. H. L. Marriott and Dr. D. G. James had a demonstration of sarcoidosis, Dr. Ray Bettley and Dr. E. A. Fairburn of malignant lymphomata of the skin, and Prof. P. B. Ascroft of the late effects of 'Thorotrast.' On the borderline between radiology and neurology, Miss Diana Beck and Mr. F. L. Davies are examining the effects of 'Myodil' on the nervous system, and Prof. B. Windeyer, with Dr. A. M. Jelliffe and Mr. Davies, those of pituitary ablation (in the dog) by injection of radioactive substances. The other exhibits included one on the toxic effects of tricresyl phosphate, which Dr. F. Hobbiger has demonstrated by inducing demyelination in hens.

## SUPERANNUATION FOR THE GENERAL PRACTITIONER

THE regulations governing the National Health Service are so many, and so complex, that doctors cannot be blamed for ignorance of most of them. The superannuation regulations for general practitioners are explained by Mr. Hugh Barry in an inexpensive booklet [1] which covers all aspects, including, for example, the provision for dependants if the doctor dies suddenly, what money he can expect if he is permanently incapacitated, and the size of his pension.

## NATIONAL INSURANCE AND TRADE UNIONS

LOCAL tribunals are set up under the National Insurance Act to hear appeals against decisions given by insurance officers. Under new regulations [2] which came into force on Dec. 3, an association of employed persons, such as a trade union, now has a right of direct appeal to the National Insurance Commissioner from a decision of a local tribunal when the association is acting on behalf of the next of kin of a deceased member on a claim for benefit arising from the member's insurance. Such associations already have this right where acting on a member's behalf.

1. Superannuation for the General Medical Practitioner in the National Health Service. London: Heinemann. 1955. Pp. 21. 2s. 6d.
2. National Insurance (Determination of Claims and Questions) Amendment Regulations, 1955 (S.I. 1955, no. 1788). H.M. Stationery Office. 3d.

## APPROVED NAMES FOR DRUGS

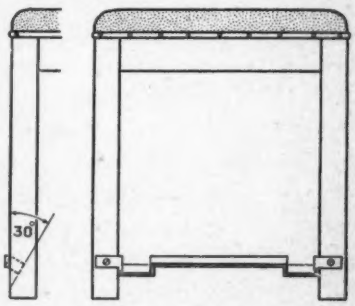
THE British Pharmacopœia Commission has issued the following new supplementary list of approved names:

| *Approved name* | *Other names* |
|---|---|
| Acetazolamide | 2-Acetamido-1:3:4-thiadiazole-5-sulphonamide. Diamox. |
| Aminometradine | 1-Allyl-6-amino-3-ethyl-1 : 2 : 3 : 4-tetrahydropyrimidine-2 : 4-dione. Mictine. |
| Benactyzine | 2-Diethylaminoethyl benzilate. Suavitil is the hydrochloride. |
| Chlorpheniramine | 1-*p*-Chlorophenyl-3-dimethylamino-1-2'-pyridylpropane. Chlorprophenpyridamine. Chlor-Trimeton is the hydrogen maleate; Piriton is the hydrogen maleate. |
| Dipipanone | 4 : 4-Diphenyl-6-piperidinoheptan-3-one. Pipadone is the hydrochloride. |
| Phenoxymethylpenicillin | A biosynthetic penicillin formed by fermentation, with suitable precursors, of *Penicillium notatum*. Penicillin V; Distaquaine V. |
| Piperoxan | 2-Piperidinomethylbenzo-1 : 4-dioxan. |
| Prednisolone | $\Delta^1$-dehydro-hydrocortisone. Pregna-1 : 4-diene-11β : 17α : 21-triol-3 : 20-dione. Metacortandralone. Delta-Cortef; Delta-Cortril; Delta-stab; Hydeltra; Meticortelone. |
| Prednisone | $\Delta^1$-dehydrocortisone. Pregna-1 : 4-diene-17α : 21-diol-3 : 11 : 20-trione. Metacortandracin. DeCortisyl; Deltasone; Deltra; Meticorten. |
| Streptoduocin | A mixture of equal parts of Dihydrostreptomycin Sulphate and Streptomycin Sulphate. Mixtamycin. |

## FOOT-BRACING BARS FOR TRACTION COUCHES

Dr. J. B. JESSIMAN writes: "In reducing cervical-disc lesions, a considerable pull has to be exerted, and its efficacy and safety depend largely on the security of the manipulator's foothold; a foothold against a highly varnished or tubular-steel leg of a traction-couch is awkward, insecure, and not without danger.

I have designed a stirrup-type foot-stop or bracing bar which can be fixed to the traction-couch easily and quickly by means of two screws at a height from the floor suitable to receive the shoe instep ($3^1/_8$–$3^1/_4$ in.). Tubular-steel legs would, of course, require holes and bolts for fixing. The bar, made of toughened steel strip, 1 by $^1/_8$ in., is cranked or stirruped and angled to 30 degrees to hold the instep of the manipulator's shoe close to the inside of the couch legs (see accompanying figure). An alternative type has adjustable stirrups which are made in two pieces, secured by thumb-screw bolts."




Both types of apparatus are obtainable from Messrs. Allen & Hanburys, 48, Wigmore Street, London, W.1.

## FILM ON BLOOD-TRANSFUSION

A FILM on blood-transfusion (16 mm., sound, colour, 24 minutes) has been made by Cyril Jenkins in collaboration with the North London Blood Transfusion Service. The first part deals with the hazards of transfusion, listing the risks arising from the donor, the stored blood, the laboratory, the transfusion itself, and the patient. This is an unsatisfactory section; for some twenty hazards are listed against a diagrammatic background, and the reading of them becomes tedious. Indeed the information could be presented more conveniently and cheaply in a printed leaflet. The larger section of the film is devoted to a brief review of giving-sets in use or planned for use in Great Britain, and a detailed demonstration of the procedure of putting up a transfusion with the "needle-piercing" set. Although at present in use in two regions, this set is not (nor is it likely to become) generally available, and it would have been preferable to demonstrate a standard giving-set. The film ends with suggested sites for transfusion (including the arm, ankle,

sternum, and, in babies, scalp veins) and a summary. The colour photography and the exposition are of a high standard, and some valuable sequences are included. The film may be borrowed free of charge from the I.C.I. Film Library, Imperial Chemical House, Millbank, London, S.W.1.

### DOCTOR AND ADMINISTRATOR

IN 1924 Duke Alberto Denti di Pirajno began his work in the Italian North African colonies by opening a dispensary at Buerat el Hsun, the small outpost in Tripolitania to which he had accompanied the exiled Duke of Aosta as physician. As his book shows, Denti proved himself an enterprising doctor, well able to deal with his varied and unorthodox patients. He was equally at home, and equally welcome, in a pasha's palace, a bedouin tent, and a Tunisian harem, and his case-histories would make any respectable card-index curl up in amazement. But, through his knowledge of the desert peoples, he was increasingly and unwillingly drawn into the work of administering the colony, and we leave him in a sad chapter as governor of Tripoli surrendering the city to General Montgomery.

## University of London

Mr. Ralph Shackman, senior lecturer at the Postgraduate Medical School of London, has been appointed to the university readership in surgery at that school.

Mr. Shackman qualified from St. Bartholomew's Hospital in 1933, taking the M.B. Lond. the following year and his F.R.C.S. in 1936. Meanwhile he held house-appointments at the Metropolitan Hospital, London, and the Royal Infirmary, Sheffield, where he later became R.S.O. He returned to London as first assistant in the department of surgery at the British Postgraduate Medical School. He also held a clinical assistantship at St. Peter's Hospital for Stone. During the late war he served as a surgical specialist with the R.A.F. medical service with the rank of wing-commander. Mr. Shackman is surgeon and urologist to Hammersmith Hospital and his publications include a paper on bladder cancer.

## Royal College of Surgeons of England

At a meeting of the council on Dec. 8, with Sir Harry Platt, the president, in the chair, Mr. E. C. B. Butler and Mr. S. H. Wass were admitted to the court of examiners.

The following lecturers were appointed for 1956: Dr. William Brockbank, Thomas Vicary lecturer; Mr. S. A. S. Malkin, Robert Jones lecturer; Mr. B. W. Fickling, Charles Tomes lecturer.

Prof. A. E. W. Miles was appointed hon. curator of the odontological museum.

Diplomas of fellowship were granted to the following:

Philip Henson, H. B. Wright, W. de M. Kellock, L. F. Levy, R. H. B. Mills, P. P. Philip, R. R. Davis, R. R. L. Pryer, D. J. Cowan, Frank Ashton, Werner Stern, † D. F. N. Harrison, Bernard Lytton, J. J. B. Hobbs, M. P. Ward, B. O. Smith, J. C. N. Wakeley, A. E. Wheatley, D. R. Sweetnam, J. A. Williams, S. A. Seligman, J. W. Bradbeer, J. G. Roberts, David Tanne, James Watt, Montague Modlin, Shakuntala Prem Chandra, Bernard Cashman, E. R. Price, Johannes Christiaan Kotzé, Himangsu Sekhar Lahiri, * E. M. L. Evans, B. B. Hall, P. B. Lacy, D. A. Larnder, Krishnadas Ray, D. C. D'Netto, J. L. Hayward, E. G. G. Jonas, * B. R. Jones, † G. E. Mann, F. O. W. Wilkinson, J. J. Connors, † R. P. Freeman, P. H. Lord, R. D. Marshall, T. W. Milliken, J. E. Mitchell, P. W. Mitchell, R. B. J. Peiris, * Dhanwant Singh, E. A. Allcock, N. C. Azizkhan, S. L. Barron, F. G. Bell, W. L. Elrick, A. R. Epstein, J. B. Fethers, D. E. Gunatilleke, Neil Johnson, Daniel Lenaghan, Leslie Linder, I. F. McNeill, J. A. Muscat, David Roux, Ary Blesovsky, Miles Fox, Joseph Hon Yin Fung, J. H. Heslop, Sibendra Mohon Lahiri, K. J. McCarthy, W. B. Maguire, I. N. Nunn, B. M. O'Brien, R. C. Shepherd, F. I. Bishop, Ronald Dee, A. J. Duke, A. F. Masson, R. W. D. Middleton, J. M. Nield, K. B. Orr, B. S. Purssey, W. W. Richardson, P. R. Robertson, Thamotheram-pillai Kangesan Shakespeare, Hiran Sirikantha-Kirthi Singha, C. C. Wiggishoff, J. D. N. Yelland, Kalyumali Abbasbhai Anjarwalla, R. L. B. Beare, R. G. Burwell, P. S. Reay-Young, R. G. Rushworth, F. C. Walker.

* In ophthalmology.
† In otolaryngology.

## Royal College of Physicians of Ireland

On Dec. 2 the following were admitted licentiates in medicine and midwifery:

Lemboye Adenia Ayorinde, Dorothea L. Baxter, P. J. Bugler, F. G. Connolly, L. M. Cusack, Hareeduth Ghoorah, Adisa Rahman Jinadu, R. E. Knight, Hana L. Malbsha, J. S. Mills, Marcus Molony, Terence MacMahon, W. V. O'Grady, Rosemary W. Orr, Pamela M. Fox-Russell, Oscar Singer, C. F. Dundas.

## Royal College of Surgeons in Ireland

At recent examinations the following were successful:

*D.C.H.*—N. J. Choksey, Marie T. Hyde, Mary P. Kent, A. J. M. X. Kerrigan, M. L. Magotra, Elinor D. U. Powell.
*D.A.*—P. Coleman, W. W. Deacon, N. Mark, G. A. Walsh, M. W. Abrams, J. B. La Grange.

1. A Cure for Serpents. Alberto Denti di Pirajno. London: Deutsch. 1955. Pp. 203. 16*s*.

## University of Dublin

On Dec. 8 at the School of Physic, Trinity College, the following medical degrees were conferred:

*M.B., B.Ch., B.A.O.*—Dolapo Ayinla Akisanya, B. C. Anyakwo, R. I. Clingen, E. H. Crennell, D. W. D. Evans, Gordon Fletcher, N. H. Fletcher, J. T. Gaston, C. W. J. Hart, J. J. Hazlett, C. J. Higgins, J. L. Hyslop, D. L. Kelly, J. R. Marshall, J. B. W. Maxwell, Nissim Armando Nassim, Patricia E. O'Neill, C. G. C. Petit, M. B. C. Reidy, I. B. Sangmuah, Monica W. Taylor, J. A. C. Terry, Laurence Warke.

## British Association of Otolaryngologists

At the annual general meeting held on Dec. 2, the following were elected officers of the association: Mr. I. Simson Hall, president; Mr. V. E. Negus, immediate past president; Mr. C. Gill-Carey, vice-president; Mr. J. C. Hogg, hon. treasurer; Mr. Myles L. Formby, hon. secretary.

## Public Relations

The Central Council for Health Education is to hold a seminar on this subject for medical officers of health at St. John House, London, S.W.7, from Feb. 28 to March 3. The programme will cover relations with the Press, contact with local organisations, and the free flow of information on health matters to the public. A study will also be made of the use of reports, handbooks, and exhibitions. Further particulars may be had from the council, Tavistock House, W.C.1.

Volume 3 of the Collected Papers published by the Laboratory Animals Bureau contains the proceedings of a symposium, held in London last May, on the Breeding of Laboratory Animals. Copies (7*s*. 6*d*.) may be had from the bureau, M.R.C. Laboratories, Holly Hill, London, N.W.3.

# Diary of the Week

DEC. 18 TO 24

### Monday, 19th

HUNTERIAN SOCIETY
8.30 P.M. (Talbot Restaurant, London Wall, E.C.2.) Dr. Evan Bedford and Mr. T. Holmes Sellors: Scope of Cardiac Surgery.

### Tuesday, 20th

INSTITUTE OF NEUROLOGY, National Hospital, Queen Square, W.C.1
5.30 P.M. Prof. David Slome: Physiology of Pain.
INSTITUTE OF DERMATOLOGY, Lisle Street, W.C.2
5.30 P.M. Dr. H. T. H. Wilson: The Erythrodermias.
ROYAL ARMY MEDICAL COLLEGE, Millbank, S.W.1
5 P.M. Dr. D. P. Cuthbertson: Food and the Future.

### Wednesday, 21st

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1
8.15 P.M. *General Practice.* Dr. Leonard Roodyn and Dr. Mary Barber: Staphylococcal Infection.
INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. Henry Haber: Reticulosis.

# Appointments

GIBSON, R. V., M.B. Camb., M.R.C.P.: asst. cardiologist, Hospitals for Diseases of the Chest, London.
KNIGHT, G. W., M.D. Leeds, D.P.H.: deputy county M.O. and deputy principal school M.O., Bucks.
MILLER, H. G., M.D. Durh., M.R.C.P., D.P.M.: physician in neurology, Royal Victoria Infirmary, Newcastle upon Tyne.
SHARP, MARY K., M.R.C.S.: asst. county and school M.O., West Riding of Yorks.
THOMPSON, MALCOLM, M.D. Durh., M.R.C.P.: physician in physical medicine, United Newcastle upon Tyne Hospitals.
TURNEY, J. P., M.B. Lond., F.R.C.S.: whole-time senior casualty officer, S.E. Northumberland H.M.C.
TYNER, R. M. C., M.B. Dubl., D.P.H.: senior M.O. for mental health, Derbyshire.
VAUGHAN, B. F., M.B. Brist., D.M.R.D.: asst. radiologist, Royal Perth Hospital, Perth, Western Australia.
WALKER, R. B., M.R.C.S., D.P.H.: M.O.H. and asst. county M.O., Kingsbridge and Salcombe U.D.S, and Kingsbridge and Blympton R.D.S.

**The Hospital for Sick Children, Great Ormond Street, London:**

SUTCLIFFE, JOHN, M.B. Camb., M.R.C.P., F.F.R., D.M.R.D.: part-time deputy director of the department of diagnostic radiology.
PAMPIGLIONE, GUISEPPE, M.D. Rome: part-time consultant physician in charge of the electro-encephalographic department.

# Births, Marriages, and Deaths

### MARRIAGES

VAUGHAN—AINSBURY.—On Dec. 1, at St. Mary's Church, Cheadle, Cheshire, Dr. Bernard Francis Vaughan to Barbary Ainsbury.

# THE SEAT OF CONSCIOUSNESS

ERIC TURNER
M.B. Glasg., F.R.C.S.
ASSISTANT NEUROSURGEON, QUEEN ELIZABETH HOSPITAL, BIRMINGHAM

Or like stout Cortex, who, with regal "I,"
Stared at the non-specific—and his random
Spikes set up a synchronitic cry,
Aghast, upon a new Symposium.

THE time seems appropriate for someone to take up a pen in defence of the cerebral cortex before it suffers any further derogation; for we are witnessing a phase in scientific thought in which it appears in danger of being relegated to a place of secondary importance.

We, of a generation brought up on the neat little areas of Campbell, Brodmann, von Economo, and the Vogts, find this disturbing. It is true that the integration between these neat parcels, each with its discrete function (not always yet allocated), was by no means clear; for, although there were connections between them, the decision as to what parcel would be attended to or controlled belonged to the will; and where the will resided, and how it exerted its influence, were relegated with other ultimate mysteries to the hinterland that lay between science and religion.

## Progress of Neurophysiology

One of the first discoveries that led ultimately to the new way of thinking about the physiology of the brain was that of Forbes and Morison (1939), who found that, under anæsthesia, a stimulus applied to the sciatic nerve produced not only a specific cortical response in the appropriate projection-area but also, after a latent period, a secondary discharge which was a diffuse response of the whole cortex.

The work that followed grew, slowly at first, until last year the Council for International Organisations of Medical Sciences produced a symposium entitled at first "The Laurentian Symposium on the Electrical Activity of the Cortex as Affected by the Brain Stem Reticular System in Relation to States of Consciousness," and later simply "Brain Mechanisms and Consciousness." The highlights of progress up to this point are familiar to most workers in neurophysiology.

The Morisons and Dempsey (1941) had found that this secondary response of Forbes and Morison could be obtained by stimulating brain-stem structures, and their discovery of a "recruiting response" on stimulation of intralaminar nuclei of the thalamus made Morison and Dempsey (1942) suggest that there might be a non-specific thalamocortical system with diffuse connections. This system was named the thalamic reticular system by Jasper (1949), who found that stimulation of it had a controlling effect on "spontaneous" cortical activity.

Moruzzi and Magoun (1949) and many collaborators have shown that a reticular activating system exists in the brain stem and that, on stimulation of it, a "desynchronisation" of electro-encephalographic potentials takes place, with arousal of the animal. Destruction of this reticular formation lowers the level of consciousness to a state resembling permanent sleep.

The upward prolongation of the reticular formation of the stem is still in doubt. Similar electrical responses and a similar arousal have been elicited by stimulation of subthalamic structures, but stimulation of the diffuse projection-system of the thalamus, while altering the electro-encephalographic patterns, has had contradictory effects on the state of wakefulness of the animal.

Meanwhile the cortical projections from specific relay and association thalamic nuclei have been meticulously worked out, and Bailey and von Bonin (1951) demonstrated that the maps of these cortical projections corresponded to constant histological zones in the cortex. They depicted a simpler cortical map than the previous ones, with transitional zones between the broadly differentiated areas. Simple cortex appeared at the base, lying posteriorly in the frontal lobe and medially along the temporal base. This they called allocortex, and it was found to form an interconnected structure with pronounced vegetative functions, the vascular and respiratory systems being affected by stimulation of it.

The stage was set generally for relegating the cortex to an inferior rôle in cerebral integration, and Penfield (1952) postulated, on philosophic grounds, a centrencephalon, whose detailed anatomy was not formulated but whose function was to act as the "highest level of functional integration." Such, he said, could not take place in the cortex, and he embraced in the centrencephalon all those parts of the higher brain stem which had symmetrical connections with both hemispheres.

## Definitions of Consciousness

Much discussion has taken place about the significance of these new ideas in relation to consciousness. In a search for the seat of consciousness much of the argument depends on the definition of consciousness. Definitions of it are numerous. They incorporate such ideas as awareness of external and internal environment; awareness of the awareness of environment; integration of sensory stimuli, with selective attention to some of them; abstraction of the integration; comparison of the present sensory pattern with memory traces of past ones; the occupation of the conscious awareness with a grossly limited number of "impressions" at a time; continuity of successive "impressions" in time either by reason of successive external sensory stimuli or by internal forces of association of fortuitous memory or abstractive logic; and the direction of successive "impressions" by forces at least partly emotional in origin. It must be admitted that all these properties are necessary for the most generalised description of human consciousness; yet, wide though the definition may seem, if it is adhered to it will prevent such confusion as arises when the intelligent reaction of an animal, either whole or maimed, to its environment is mistakenly taken as having any bearing on consciousness, as here defined, which must necessarily, by the laws of empirical science, be a human characteristic.

In an excellent discussion of such problems Fessard (1954) concludes that the phenomenon of consciousness can be succinctly defined as "experienced integration." He suggests that the locus of such experienced integration may be one of three sites: the brain as a whole; the cortex as a whole; or a specific region of the brain, the other parts of the brain participating only in the form of unconscious operations.

The only other suggestion is one derived from William James (1890). It has been referred to by Sherrington (1906) as well as Fessard, but though oft quoted it is so quotable that I bow to these masters and repeat the reference to the "privileged integrating neurone, one ultimate pontifical cell."

At this point Fessard begins to show serious consideration for the third view and, for one possible region of experienced integration, goes down (or, as Penfield (1954a) might say, up) to the brain stem and the reticular substance. Fessard's reasons for doing so are interesting; they include reports of experiments on animals (always a trap in relation to consciousness) and of the physiological as well as the anatomical results of these.

Lashley's (1950) work is cited, for he found that cortex isolated from surrounding parts of the grey matter could still allow intelligent response by an animal to sensory stimuli. This led to the conception of "isopotentiality of cortex," which was thought to play a relatively non-specific rôle in relation to the diencephalon.

Magoun's (1954) results are also taken as pointing towards the reticulum as a possible major integrative structure. Both Lashley and Magoun seem to be less impressed than others by this interpretation of their own work: Magoun expresses doubt about it; Lashley says flatly that he does not see any reason to believe it. The reticulum does not yet seem to have been shown to possess either the quality of patterning or the correct anatomical connections for such a job—indeed its connections are too numerous and diffuse rather than too few.

Language is inseparable from the demonstration in others of fully developed consciousness, and no brain-stem preparation, whether human or animal, can give this demonstration. (Penfield (1954b) admits that cortex is necessary as a kind of appendage to the centrencephalon.) Furthermore, if equipotentiality of cortex has some meaning for crude experiments on immature animals, it does not have the same meaning for the cortex of adult human beings, as I, as a neurosurgeon, know to my cost.

However, it may be preferable to look at the problem in a positive way instead of dwelling on the insufficiencies of the reticular substance as a net "to catch a soul in."

## Criteria of Consciousness

If we analyse the phenomena that have been described we see that three criteria are necessary to comprehend full consciousness with the attributes that have been outlined above.

*Vegetative Consciousness*

(1) The first criterion might be called vegetative consciousness—the fact that the person must be awake at the time. For this the brain stem, complete with reticulum, is necessary, as has been experimentally proved not only in animals but also clinically in man. At first sight this may seem no more significant than saying that to do well in an examination it is preferable for the candidate not to be under a general anæsthetic at the time. There is, however, more to the subject than that, for the descending projections to the reticulum have yet to be worked out and are certainly of importance, for the significance as well as the strength of stimuli contributes to their arousal value, as when a person awakens in response to his own whispered name or to the whimper of a sick child.

*Empirical Consciousness*

(2) The second criterion represents the integrative level of thought and might be called empirical consciousness. The word "empirical" applies in both its active and its passive senses, for it is the level at which the environment is dealt with on an empirical basis and at which an observer can become convinced that some of the phenomena of consciousness are occurring by reason of empirical data, particularly in the sphere of language. Memory is necessary at this level, together with direction of attention and of the sequence of thought. The integrative locus must therefore be subject to incoming stimuli, must have available memory traces, and must be capable of influence by directive forces, including emotional ones.

It has long been thought that the association-area of cortex in the temporo-parietal lobe of the dominant hemisphere fulfils the criteria demanded for empirical consciousness. It meets the demands that Fessard made for a region of experienced integration, and it is known that even the simple sensory projection-areas of cortex show experimentally all the properties required for this integrative function. It also possesses the unity required to ensure that only one dominant pattern can occupy it at any one moment, with a very few secondary patterns reaching subliminal values. In the closely adjacent temporal areas auditory sensory association cortex has to translate temporal sequences into spatial ones to find significance in them; so it is natural that experimental demonstration by temporal stimuli of functions of memory should be most easily demonstrated here, though it is probable that other sensory modalities have their own less overt properties of memory. All are in direct continuity with the cortical area in question.

*Abstractive Consciousness*

(3) The third criterion for full consciousness is a second order of integration representing abstractions based on the data of the "empirical area." This might be called abstractive consciousness, and here the difficulties have arisen. The frontal cortex has strong claims to be considered the main cortical area subserving abstractive functions; but how is attention widened at times to include its abstractive activity, and how at other times is it narrowed to exclude this second order of integration?

> "When one is acting in an extreme emergency," says Lashley, "there is consciousness confined almost entirely to the environment."

If the function of abstractive areas may be compared with the frequency analyser on an electro-encephalograph, which can act only on the wave-forms produced in the other channels, and only if it is connected to a channel and switched on, may we look in the brain for a connector and switch?

Up to now such a search would be considered fantastic, but let us examine the discoveries that have led to the recent change in views. The reticular substance and the diffuse and specific projection-systems of the thalamus represent suitable effector mechanisms whereby one dominant associative area of cortex could influence the rest, provided it could get the appropriate messages through to them. There must be a directive force as well as a directive pathway, and this brings our attention to the medial structures of the temporal lobe.

## Medial Structures of Temporal Lobe

The current theories about these do not appear to be of much help.

Papez (1937) thought that the figure-of-eight circuit of hippocampus, fornix, mammillary bodies, anterior nucleus of thalamus, and cingulate gyrus represented a system for the "prolongation of emotional states."

MacLean (1952) sees in the hippocampus and the overlying cortex parts of a "visceral brain." He claims that all modalities of sensation enter it, and it is therefore capable of being a centre of major importance in the system of vegetative control that he describes. Unfortunately, cutting of the fornix has been singularly disappointing in producing temperamental changes in animals, and Pribram and Fulton (1954) say that removal of the hippocampus fares no better.

What does produce a gross change in temperament is either removal of the temporal-lobe cortex bilaterally or else destruction of other pathways passing from it towards the brain stem. The hippocampus and fornix, if they are freed from direct vegetative projection, are eminently capable of fulfilling a more subtle function.

Herrick (1933) set this particular ball rolling with the suggestion that the rhinencephalon might have taken over the function of a non-specific activator of all cortical activity, "lowering its threshold or increasing its sensitivity, or exerting inhibitory influences. Thus, it might influence behaviour in the form of learning capacity, memory, &c., as a differential influence upon cortical and subcortical functions. Having no localising pattern of its own it may yet act on systems which have." Prophetic words.

Green and Arduini (1954) put another fragment into the jigsaw puzzle. They found that stimulation of the ascending reticular substance caused electro-encephalographic changes in the hippocampus; but, when the isocortex was desynchronised by this means, the hippocampus was synchronised at 5–7 cycles per second (the closest correspondence to α rhythm that an animal possesses) and vice versa. This explains the apparently

diverse afferent system of the hippocampus, which is non-specific and reaches the hippocampus in retrograde fashion via the fornix, most of whose fibres pass towards the hypothalamus.

### Conclusion

When, with all this in our minds, we look down into the deep cleft of a surgical exposure of the temporal horn of the ventricle, perhaps we do not now see the hippocampus looking so much like a sea-horse as it once did. Wait till we dam the rising tide of cerebrospinal fluid and pull aside the choroidal seaweed, and then we have been led to expect the hippocampus, like Proteus, to take almost any animate guise. Yet it may be just as much akin to the keyboard of an instrument as to a fish. Could one stretch the metaphor to include the hippocampal gyrus sitting on a stool before that keyboard, sending messages prompted by the neighbouring convolutions? One could imagine the orders coming through: "Repeat till memorised," "Concentrate, *please!*", "You may stop your abstract thinking now, a bomb has just dropped through the roof."

But let us not stretch a figure of speech beyond the limits of its usefulness. Let us not toy with such ideas as that "silent" areas are not really silent but only ambidextrous; let us not speculate on whether disturbance of such a system of internal communication on a functional or an organic basis might lead to a state resembling schizophrenia; and let us not picture the littérateur using the abstractive areas of his temporal cortex when he uses language to convey emotional inexpressibles. If we refrain from these temptations we may be spared the necessity of explaining away bilateral synchrony of the basal temporal lobes, for the anterior commissure and the others available seem inadequate for point-to-point projection and could carry only a brief summary across the midline. Perhaps the messages are indeed so simple that a greetings telegram would suffice.

However, any alternative would take us back to the reticulum of the brain stem; so we should perhaps take refuge in dignified silence.

#### REFERENCES


Bailey, P., von Bonin, G. (1951) *Ill. Monogr. med. Sci.* **6**, 1 and 2.
Fessard, A. (1954) *In* Brain Mechanisms and Consciousness. Oxford; p. 200.
Forbes, A., Morison, B. R. (1939) *J. Neurophysiol.* **2**, 112.
Green, J. D., Arduini, A. A. (1954) *Ibid*, **17**, 533.
Herrick, C. J. (1933) *Proc. nat. Acad. Sci. Wash.* **19**, 7.
James, W. (1890) The Principles of Psychology. New York.
Jasper, H. H. (1949) *Electroenceph. clin. Neurophysiol.* **1**, 405.
Lashley, K. S. (1950) *Symp. Soc. exp. Biol.* **4**, 454.
MacLean, P. (1952) *Electroenceph. clin. Neurophysiol.* **4**, 407.
Magoun, H. W. (1954) *In* Brain Mechanisms and Consciousness. Oxford; p. 1.
Morison, R. S., Dempsey, E. W. (1942) *Amer. J. Physiol.* **135**, 281.
— — Morison, B. R. (1941) *Ibid*, **131**, 732.
Moruzzi, G., Magoun, H. W. (1949) *Electroenceph. clin. Neurophysiol.* **1**, 445.
Papez, J. W. (1937) *Arch. Neurol. Psychiat., Chicago*, **38**, 725.
Penfield, W. (1952) *Res. Publ. Ass. nerv. ment. Dis.* **30**, 513.
— (1954a) *In* Brain Mechanisms and Consciousness. Oxford; p. 286.
— (1954b) *Ibid*, p. 307.
Pribram, K. H., Fulton, J. F. (1954) *Brain*, **77**, 34.
Sherrington, C. S. (1906) The Integrative Action of the Nervous System. 1947 ed., Cambridge; p. 381.


". . . I regard it as desirable that men should enjoy an ever-increasing flow of goods; I am far more doubtful about the successive reduction in hours of work. When prophets of the future speak of a thirty-two hour week, to be followed in time by a twenty-four hour week, I wonder whether they are not missing the main point. No man can desire the reduction of his working week to thirty-two and then to twenty-four hours unless he dislikes his work. No scientist will take kindly to the suggestion that he may spend only thirty-two and then twenty-four hours in his laboratory. This then points out to us what I regard as the real problem of the future: to make work enjoyable. Would that not be a greater contribution to man's happiness than to whittle down the hours? In fact this whittling down is called for only because work is not enjoyed, and no man can be called happy who is not happy in his work."—BERTRAND DE JOUVENEL, *Listener*, Dec. 15, 1955, p. 1032.

## INGUINAL HERNIORRAPHY*


F. S. A. DORAN
M.D. Camb., F.R.C.S.
SURGEON, MID-WORCESTERSHIRE HOSPITALS


DESPITE an ever-growing volume of criticism, most inguinal herniæ are still repaired by techniques with a central common factor—the rearrangement of the lower border of the conjoint tendon (inguinal aponeurotic falx). This rearrangement is of two types: the lower border of the conjoint tendon is sewn either to the inner surface of Poupart's (inguinal) ligament or to Cooper's (pectineal) ligament, which is attached to the pecten pubis and arcuate line. The success of this kind of herniorraphy presumably depends on achieving a secure permanent union between the conjoint tendon and the ligament to which it has been sutured.

It is a surgical axiom that tissues sewn together under tension are unlikely to remain permanently united, because the sutures will cut out, or the scar forming the union will weaken and stretch. Fifty years ago Halsted (1903) suspected that the degree of tension needed to bring the conjoint tendon into contact with Poupart's ligament was dangerously high and a cause of failure after this type of operation. That this suspicion was well founded is supported by the fact that, when a recurrence is explored, the conjoint tendon is no longer attached to the ligament upon which it had been sutured down.

Gallie and Le Mesurier (1921, 1924), reporting observations on a large number of recurrences following Bassini's operation, stated that "in every instance, the aponeurotic structures that had been sutured to the ligament had returned to their normal positions."

Workers from Fergusson (1907) to Mair (1945) have expressed the opinion that, if an appreciable amount of tension is present when the conjoint tendon is sewn to the ligament, a sound permanent union is unlikely, and there will probably be a recurrence.

Indeed, it has been demonstrated, by means of radio-opaque markers inserted into the conjoint tendon above and into either Poupart's or Cooper's ligament below, that these structures resumed their preoperative relationship within six months in 60% of the cases tested (Doran and Lonsdale 1949).

That the degree of tension present when the conjoint tendon is sewn down on to either Poupart's or Cooper's ligament, may be dangerously high is surprising because the integrity of the inguinal canal is supposed to depend partly on the conjoint tendon descending "shutter-like" to lie "pressed against and flush with Poupart's ligament, thus closing the inguinal gap" (Keith 1924). In other words, when the muscles of the abdominal wall contract, it is "natural" for the conjoint tendon to lie in apposition with Poupart's ligament. The notion of strengthening the inguinal canal by maintaining the "shutter" in the "closed" position therefore seems to possess anatomical and physiological sanction; but as a matter of fact this concept of the part played by the conjoint tendon in supporting the integrity of the inguinal canal is incorrect.

### "Shutter" Action of Conjoint Tendon a Myth

The inability of the conjoint tendon to act like a "shutter" in the way described by Keith (1924) has been pointed out by several surgeons (Cole 1941, Brandon 1946, Patey 1949). The anatomy of that part of the anterior abdominal wall (below the level of the anterior superior iliac spines) in which the inguinal canals lie leaves little doubt that, in most instances, the conjoint tendon cannot act like a "shutter" or be approximated passively to either Poupart's or Cooper's ligament without tension. The evidence supporting this statement is both anatomical and experimental.

* Based on a paper read to the Anatomical Society of Great Britain and Ireland on April 22, 1955.

*Anatomical Evidence*

The "arch" described by the lower border of the internal oblique muscle and the conjoint tendon (inguinal aponeurotic falx) over the inguinal canal is fixed laterally to the outer half of the inguinal ligament, from which the internal oblique muscle arises, and medially to the crest of the os pubis and the pecten pubis, into which the conjoint tendon is inserted. This "arch" is not an independent structure but is the lower edge of a musculo-aponeurotic sheet which forms a layer of the anterior abdominal wall.

In a normal person, on coughing or straining, the anterior abdominal wall (both sides acting in unison) contracts, thereby constricting the abdominal cavity. Since the contraction of the muscles in the right half of the abdominal wall is balanced by that of the muscles in the left half, the linea alba, into which the two internal oblique muscles are principally inserted, remains in the midline. Therefore the point on the linea alba (at the level of the anterior superior iliac spines) into which the internal oblique muscle runs horizontally from that bony origin must remain equidistant from the right and left anterior superior spines. Moreover, with a person standing upright, the attachments of the linea alba remain the same distance apart when the abdominal wall contracts. The point on the linea alba opposite the anterior superior spines therefore does not move up or down. Since this point (X in fig. 1) does not move in the coronal plane it has been called the primary fixed point.

For all practical purposes, therefore, that part of the anterior abdominal wall distal to a line joining the anterior superior spines can be regarded as consisting of two inelastic triangles (XYZ and XWZ in fig. 1) each containing an inguinal canal. Fig. 1 shows that the centre of the "arch" (B and $B^1$) can only touch the opposite point on the inguinal ligament (C and $C^1$) under two conditions: (1) where the tissue between the "arch" and the linea alba is elastic; and (2) where contraction of the muscles on one side of the linea alba is associated with relaxation of those on the other, allowing the linea alba to be pulled away from the midline. Neither of these two conditions existed in any of the patients tested, in spite of the fact that the tissue joining the "arch" to the linea alba contains elastic fibres (Lunn 1948).

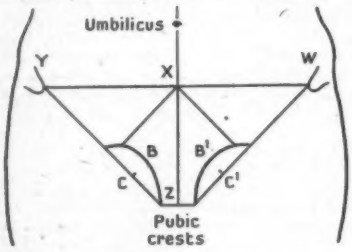



**Fig. 1—The point X on the linea alba being fixed in both planes by the opposing contractions of the horizontal fibres of the internal oblique muscles, YX and WX, it is impossible for the points B and $B^1$ on the "arches" to descend on to C and $C^1$ on Poupart's ligament, particularly since the tissue between the linea alba and B and $B^1$ is inelastic.**

On anatomical grounds the conclusion is inescapable that the "arch" of the internal oblique aponeurosis and the conjoint tendon over the inguinal canal is inflexible and plays no part in maintaining the integrity of the canal.

*Experimental Evidence*

(1) Patey (1949) described the direction in which those fibres of the internal oblique muscle that arise from the outer half of the inguinal ligament pull as they contract. He observed that, when stimulated electrically, the fibres of the internal oblique muscle which had reached the top of the "arch" pulled in a line parallel to the inguinal ligament, and that there was no "shutter" action by the conjoint tendon. In 25 patients with inguinal hernia I repeated this experiment and confirmed Patey's observation in each case.

(2) Six patients operated on for hydrocele had a radio-opaque marker inserted in the centre of the "arch" and another marker in the inguinal ligament directly opposite to it. At a later date these patients were radiographed first with the abdominal muscles relaxed and then with the muscles contracted. The markers did not come together in any of the six patients tested.

These observations confirm the conclusion reached on anatomical grounds that the "shutter" action of the internal oblique aponeurosis and the conjoint tendon on to the inguinal ligament is a myth.

### Halsted-Tanner Relaxing Incision

The inflexible tissue which maintains the "arch" formed over the inguinal canal by the internal oblique muscle and the conjoint tendon and opposes the apposition of the "arch" to Poupart's ligament is the aponeurotic sheet which is divided by the Halsted-Tanner relaxing incision (fig. 2). This incision effectively overcomes the passive resistance to the proposed surgical apposition of the internal oblique tendon and the conjoint tendon either to Poupart's or to Cooper's ligament and allows that step in the operation to be effected virtually without any tension if the "arch" is being sewn to Poupart's ligament, but often with a little tension when it is sutured to Cooper's ligament.

The relaxing incision does more than overcome the passive resistance of that part of the internal oblique and transversalis aponeurosis which is inserted into the linea alba from the pubis to the umbilicus; it protects the union of the internal oblique aponeurosis and the conjoint tendon with Poupart's ligament from the relentless tug of that portion of the internal oblique and transversalis muscles which arises from the anterior superior spine on the opposite side.

When the "arch" is sewn down either to Poupart's or to Cooper's ligament without the relaxing incision, the junction is achieved by stretching the muscle-fibres of the internal oblique and transversalis muscles which arise from the anterior superior spine on the opposite side, the remaining tissues between the "arch," which the surgeon intends to displace, and the opposite internal

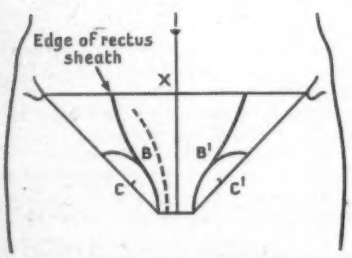



**Fig. 2—Relaxing incision through the rectus sheath divides the inelastic tissue by which the "arch" is attached to the linea alba.**

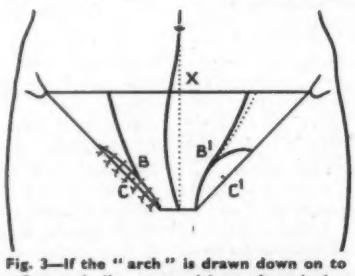



**Fig. 3—If the "arch" is drawn down on to Poupart's ligament, without the relaxing incision, the linea alba is displaced to that side.**

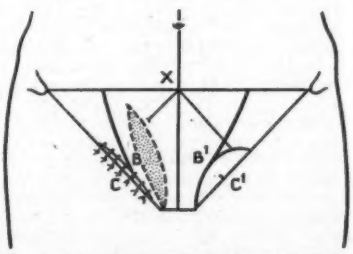
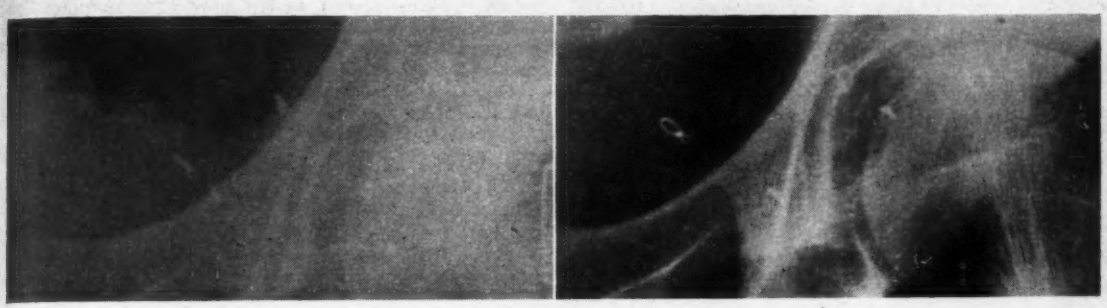
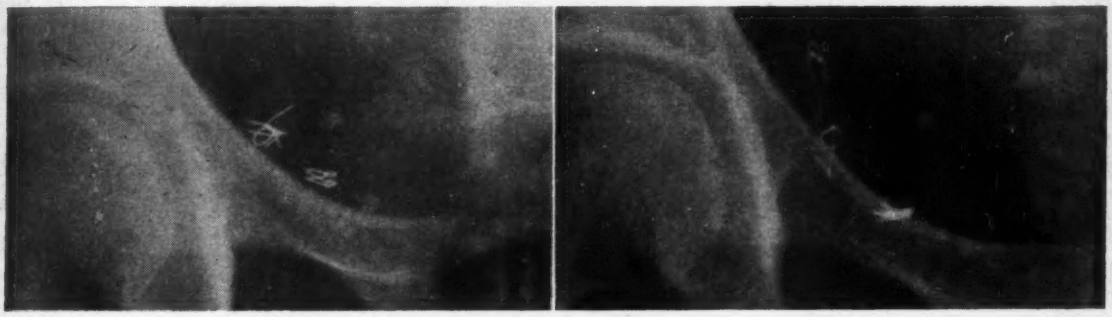



**Fig. 4—With the relaxing incision the "arch" can be drawn on to Poupart's ligament without displacing the linea alba.**



*a* *b*

Fig. 5—Positions of markers in "arch" and in Poupart's ligament: *a*, a week after operation; *b*, a year after operation (inner pair have spread widely apart).



*a* *b*

Fig. 6—Positions of markers in "arch" and in Cooper's ligament: *a*, a week after operation; *b*, a year after operation (outer pair have separated widely).

oblique muscle being aponeurotic and inflexible. It will be noted that the linea alba is displaced towards the side of the herniorraphy (fig. 3).

The operator tends to be deceived by the ease with which the conjoint tendon is often pulled down on to one of the ligaments; this absence of tension is due to the anæsthesia, which has relaxed the muscles on the opposite side of the anterior abdominal wall. An attempt to do the herniorraphy with the muscles of the anterior abdominal wall contracted and tense is salutary.

As soon as the anæsthesia has worn off, the appropriate fibres of the opposite internal oblique and transversalis muscles begin their almost ceaseless attempt to restore the linea alba to the midline; if they succeed they will do so probably at the expense of the herniorraphy. If the relaxing incision has been made, however, the linea alba is not displaced at the time of the operation; and the muscles on the opposite side have lost the continuity of the inelastic aponeurosis through which, by a relentless tug, they could pull the internal oblique aponeurosis and the conjoint tendon away from either Poupart's or Cooper's ligament (fig. 4).

Theoretically, therefore, the Halsted-Tanner relaxing incision is an essential step in promoting a permanent union between the internal oblique aponeurosis and the conjoint tendon and the ligament to which they have been sewn.

*Clinical Test*

To find out whether the Halsted-Tanner relaxing incision was as effective in practice as the foregoing theoretical considerations suggest, in a series of operations two radio-opaque markers were inserted into the lower border of the internal oblique aponeurosis and the conjoint tendon, and two similar markers were inserted into either Poupart's or Cooper's ligament in each case. These markers were radiographed in the immediate postoperative period and a year later. This test was made on 37 herniorraphies; in 25 cases the "arch" was sutured to Poupart's ligament and in 12 cases to Cooper's ligament.

It is disappointing to find that the relaxing incision cannot ensure a sound permanent union between the "arch" and the ligament upon which it has been drawn down: of the 25 cases in which the union had been to Poupart's ligament 9 had separated by the end of the first postoperative year; and of the 12 cases in which the union had been to Cooper's ligament 3 had separated at the end of the first year. 22 cases were radiographed again at the end of the second year, but in all of them the film showed no alteration from the position (either apposition or separation) which existed when the previous radiograph was taken. It therefore seems that success or failure, with regard to the union between the "arch" and the ligament, is decided in the first year after operation. Fig. 5 illustrates the separation of the conjoint tendon from Poupart's ligament, and fig. 6 its separation from Cooper's.

## Conclusions

The "shutter" action of the internal oblique aponeurosis and the conjoint tendon is a myth.

The notion of maintaining the "shutter" in the "closed" position is theoretically an unsound basis for a herniorraphy.

The object of maintaining the "shutter" in the "closed" position is difficult to achieve in practice, because even the Halsted-Tanner relaxing incision cannot ensure a firm permanent union between the conjoint tendon and the ligament, either Poupart's or Cooper's, to which it has been sewn.

I wish to thank Prof. F. A. R. Stammers, of the University of Birmingham, for his interest and encouragement and for reading the manuscript; Prof. G. A. G. Mitchell, Dr. E. Patterson, and Dr. G. T. Ashley, of the department of anatomy in the University of Manchester, for their helpful criticism and

guidance; and Dr. D. I. Harries, radiologist to the Mid-Worcestershire Hospitals, for his careful assessment of the position of the radio-opaque markers.

REFERENCES

Brandon, W. J. M. (1946) *Brit. J. Surg.* **34**, 13.
Cole, P. P. (1941) *Ibid*, **29**, 168.
Doran, F. S. A., Lonsdale, W. H. (1949) *Ibid*, **36**, 339.
Fergusson, A. H. (1907) *W. Canad. Med. J.* **1**, 3.
Gallie, W. E., Le Mesurier, A. B. (1921) *Canad. med. Ass. J.* **11**, 504.
—— —— (1924) *Arch. Surg.* **9**, 516.
Halsted, W. S. (1903) *Bull. Johns Hopk. Hosp.* **14**, 208.
Keith, A. (1924) *Brit. J. Surg.* **11**, 445.
Lunn, H. F. (1948) *Ann. R. Coll. Surg., Engl.* **2**, 285.
Mair, G. (1945) *Brit. J. Surg.* **32**, 381.
Patey, D. H. (1949) *Ibid*, **36**, 264.
Tanner, N. C. (1942) *Ibid*, **29**, 285.

# PROLONGED CHEMOTHERAPY IN PULMONARY TUBERCULOSIS

CLIFFORD HOYLE
M.D. Lond., F.R.C.P.
CONSULTING PHYSICIAN, KING EDWARD VII SANATORIUM, MIDHURST, SUSSEX; PHYSICIAN, KING'S COLLEGE HOSPITAL AND BROMPTON HOSPITAL, LONDON

HOWARD NICHOLSON
M.D. Lond., F.R.C.P.
PHYSICIAN, UNIVERSITY COLLEGE HOSPITAL AND BROMPTON HOSPITAL, LONDON

JOHN DAWSON
M.C., M.D. Lond., M.R.C.P.
SENIOR CONSULTANT CHEST PHYSICIAN, PLYMOUTH CLINICAL AREA; LATE MEDICAL CHIEF ASSISTANT, BROMPTON HOSPITAL, LONDON

IN this country the treatment of pulmonary tuberculosis with antibacterial drugs is based upon the trials of the Medical Research Council. These trials demonstrated the relative efficiency of different combinations and schemes of dosage of the three drugs in common use at the present time: streptomycin, isoniazid, and sodium *p*-aminosalicylate (P.A.S.). Also they forecast the risks to be expected from the emergence of insusceptible organisms and showed that some combinations of drugs are more hazardous than others in this respect. Although the periods of treatment used by the Medical Research Council increased from six weeks to six months they were limited by the need for achieving results in a reasonably short time. The most effective duration of treatment was not investigated.

We describe here the results in 142 patients treated by chemotherapy for nine months or longer and discuss the factors on which the duration of treatment should depend.

## Present Investigation

142 patients with pulmonary tuberculosis who had been in our care since 1950 received chemotherapy for nine months or more. No patient who completed nine months' treatment was excluded. 63 were observed for at least a year after the completion of treatment. At first prolonged treatment was given only to patients with advanced tuberculosis that could not be dealt with in any other way; later we began to use it as a routine for nearly all types of tuberculosis.

Prolonged chemotherapy was given for the following reasons:

(1) Relapse after previous treatment (57 patients).

(2) Combined with collapse treatment or resection when all disease had not been controlled (43 patients).

(3) As an alternative to surgical treatment when this was refused or was impracticable because of the situation of the disease or the age or personality of the patient (34 patients).

(4) When other treatment was impossible because of the extent of the disease or the inadequacy of the respiratory reserve (51 patients).

Some patients appear under more than one heading. Groups 3 and 4 include patients for one reason or another unsuitable for any other form of treatment. Those in group 4 are separated from those in group 3 because they had the most severe and extensive tuberculosis. The numbers in each category are analysed in table I according to the extent of the tuberculosis (see below).

### *Classification and Extent of Disease*

The classification of the patients was based upon the radiographic appearances and followed that used by Foster-Carter et al. (1952):

*Class I*: not more than one zone in one lung involved.
*Class II*: unilateral or bilateral disease involving two or three zones.
*Class III*: bilateral disease affecting four or more zones.

There were 23 patients in class I, 73 in class II, and 46 in class III (table II). There were more males than females in the ratio of 4 : 3 in the series as a whole. The predominance was entirely in class III, where there were more than twice as many men as women (table III). The mean age of the men was 37 in class I, 38 in class II, and 41 in class III, and of the women 27, 30, and 29 respectively.

### *Tuberculosis with Cavitation*

Cavities were graded according to their greatest diameter as follows: small cavities 1·0–1·5 cm.; medium cavities 1·6–2·5 cm.; large cavities 2·6–4·0 cm.; and very large cavities over 4·0 cm. If more than one cavity was present, the largest was used as the measure. 92 of the 142 patients had cavities; 27 small, 25 medium, 16 large, and 24 very large.

TABLE I—REASONS FOR PROLONGED CHEMOTHERAPY IN 142 PATIENTS

| Reason | No. of patients | | | |
|---|---|---|---|---|
| | Class I | Class II | Class III | Total |
| *Relapse after previous treatment:* | | | | |
| With either collapse treatment or resection | — | 14 | 8 | 22 |
| Chemotherapy alone | 3 | 17 | 15 | 35 |
| Combined with either collapse treatment or resection | 8 | 19 | 16 | 43 |
| Alternative to surgery | 8 | 23 | 3 | 34 |
| Other treatment impracticable | 4 | 20 | 27 | 51 |

### *Treatment*

All the patients were treated with a combination of two of the three drugs streptomycin sulphate, P.A.S., and isoniazid; 2 patients had viomycin late in their treatment when organisms resistant to the other drugs were found in their sputum; and a few other patients had dihydrostreptomycin for a time soon after it came into use.

The usual treatment for the first six to twelve weeks was intramuscular streptomycin sulphate 1 g. daily, with either P.A.S. 16–20 g. daily in four doses or isoniazid 100 mg. twelve-hourly by mouth. Patients weighing less than 9 st. were allowed to take P.A.S. 12 g. daily, but as a rule a larger dose was accepted.

When the cavities closed and sputum became free from *Mycobacterium tuberculosis*, the dose of streptomycin was reduced to 1 g. two or three times weekly

TABLE II—EXTENT OF PULMONARY TUBERCULOSIS IN 142 PATIENTS TREATED BY PROLONGED CHEMOTHERAPY

| Class | No. of patients | Number of zones affected | | | | | |
|---|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | 4 | 5 | 6 |
| I | 23 | 23 | — | — | — | — | — |
| II | 73 | — | 32 | 41 | — | — | — |
| III | 46 | — | — | — | 24 | 11 | 11 |

combined with P.A.S. daily. The change was usually made after three or four months' treatment. This régime was then continued throughout the period of treatment.

23 patients had from nine to twelve months' treatment, 76 had from twelve to eighteen months, 31 had from eighteen months to two years, and 12 had more than 2 years (table IV). Most patients rested in bed for the first three to six months, except that they were allowed to go to the lavatory once a day. They then had sanatorium treatment for another three to six months. Many patients were at home for part of the time spent in bed, especially when this exceeded three or four months.

TABLE III—AGE AND SEX OF 142 PATIENTS TREATED BY PROLONGED CHEMOTHERAPY

| Class | Males | | | Females | | |
|---|---|---|---|---|---|---|
| | No. | Age (yr.) | | No. | Age (yr.) | |
| | | Range | Mean | | Range | Mean |
| I | 13 | 16–61 | 37 | 10 | 14–39 | 27 |
| II | 36 | 15–62 | 38 | 37 | 13–57 | 30 |
| III | 32 | 25–60 | 41 | 14 | 17–46 | 29 |
| Total | 81 | | | 61 | | |

Those with medium or large cavities were nursed in hospital with the cavity dependent to facilitate closure.

Of the 142 patients 101 were treated solely by rest and chemotherapy. The remaining 41 were treated in other ways as well (table V): some form of resection was done in 16, thoracoplasty in 8, extrafascial pneumolysis and plombage in 6, artificial pneumothorax in 7, and pneumoperitoneum in 4.

*Methods of Assessment*

The traditional criteria of improvement—abatement of fever, gain in weight, a fall in the erythrocyte-sedimentation rate, control of cough, and reduction of the quantity of sputum were not used. Some are difficult to estimate accurately, and others closely accompany and depend on the dwindling population of *M. tuberculosis*

TABLE IV—DURATION OF CHEMOTHERAPY IN 142 PATIENTS

| Class | No. of patients | Weeks' therapy | | | |
|---|---|---|---|---|---|
| | | 38–51 | 52–78 | 79–104 | More than 104 |
| I | 23 | 8 | 10 | 4 | 1 |
| II | 73 | 11 | 45 | 14 | 3 |
| III | 46 | 4 | 21 | 13 | 8 |
| Total | 142 | 23 | 76 | 31 | 12 |

in the lungs, the absorption of inflammatory exudate, and the closure of cavities. These three features are the most direct guides to progress.

Improvement was therefore measured mainly by bacteriological and radiographic methods. Sputum concentrates were examined monthly and cultures made. Radiographic changes were followed with monthly postero-anterior films, and the closure of cavities with tomograms. In addition the final results of treatment were judged by the ability of the patients to resume and continue their ordinary lives.

## Results

### DURING TREATMENT

*Duration of Radiographic Change*

The radiographs of the 142 patients were examined to determine after what period of treatment there was no further alteration in the shadows in the lung. These changes comprised clearance of shadows, the substitution of linear for more diffuse shadows, and

TABLE V—TREATMENT OF 142 PATIENTS WITH PULMONARY TUBERCULOSIS

| Treatment | No. of patients | Class I | Class II | Class III |
|---|---|---|---|---|
| Prolonged chemotherapy alone | 101 | 15 | 58 | 28 |
| *Prolonged chemotherapy combined with:* | | | | |
| *Resection of:* | | | | |
| Lung | 2 | — | — | 2 |
| Lobe | 7 | 1 | 4 | 2 |
| Segment | 7 | 4 | 3 | — |
| Thoracoplasty | 8 | 1 | 2 | 5 |
| Plombage | 6 | — | 2 | 4 |
| Artificial pneumothorax | 7 | 2 | 2 | 3 |
| Pneumoperitoneum | 4 | — | 2 | 2 |
| Total no. receiving combined therapy | 41 | 8 | 15 | 18 |

evidence of contraction of parts of the lung. The closure of cavities is considered separately. The results are shown in table VI. The radiographic appearances remained unchanged in 13 (9%) of the 142 patients throughout the period of treatment. All the others improved: 18 (13%) for three months only; 38 (27%) for six months; 49 (35%) for nine months; 20 (14%) for one year; and 4 (2%) for more than one year. A third of the patients in class I, half of those in class II, and two-thirds of those in class III continued to improve radiographically after six months.

TABLE VI—DURATION OF RADIOLOGICAL IMPROVEMENT IN 142 PATIENTS TREATED BY PROLONGED CHEMOTHERAPY

| Class | No. of patients | Unimproved | Duration of improvement | | | | |
|---|---|---|---|---|---|---|---|
| | | | 3 mos. | 6 mos. | 9 mos. | 1 yr. | More than 1 yr. |
| I | 23 | 4 | 6 | 5 | 7 | 1 | 0 |
| II | 73 | 6 | 10 | 21 | 24 | 10 | 2 |
| III | 46 | 3 | 2 | 12 | 18 | 9 | 2 |
| Total | 142 | 13 | 18 | 38 | 49 | 20 | 4 |

*Closure of Cavities*

Of the 142 patients 92 had cavities more than 1 cm. in diameter. Either these were closed, or the portion of lung containing them was removed, in all the patients except 5: 1 of these 5 patients refused operation, and the 4 others were unfitted for it. 23 patients required either surgical collapse treatment or resection: 4 had small cavities, 3 medium, 7 large, and 9 very large cavities. Of the 7 small or medium cavities which did not close with chemotherapy alone 5 were several years old and

TABLE VII—92 PATIENTS WITH CAVITIES TREATED BY PROLONGED CHEMOTHERAPY. CLOSURE OF CAVITIES

| Diameter of cavity (cm.) | No. of patients with cavities | No. of patients with cavities closed by either collapse or resection | No. of patients treated with chemotherapy alone: Time of closure of cavities | | | | | | Cavities persisting |
|---|---|---|---|---|---|---|---|---|---|
| | | | Undetermined | 3 mos. | 4 mos. | 6 mos. | 9 mos. | 1 yr. | Later than 1 yr. | |
| Small, 1·0–1·5 | 27 | 4 | 7 | 8 | 4 | 3 | 1 | — | — | — |
| Medium, 1·6–2·5 | 25 | 3 | 4 | 5 | 5 | 6 | 1 | — | — | 1 (refused operation) |
| Large, 2·6–4·0 | 16 | 7 | 1 | 1 | 3 | 3 | 1 | — | — | — |
| Very large, > 4·0 | 24 | 9 | 1 | 1 | 2 | 2 | 2 | 3 | — | 4 |
| Total | 92 | 23 | 13 | 15 | 14 | 14 | 5 | 3 | — | 5 |

lay among dense shadows which were unaffected by chemotherapy; their walls were thick and clearly defined in tomograms suggesting that they were fibrotic. The 2 other cavities were excavated "tuberculomas" with thick irregular walls.

In 64 of the 92 patients (69·5%) with excavated lesions the cavities were closed by chemotherapy alone (table VII): 23 of 27 small cavities, 21 of 25 medium, 9 of 16 large, and 11 of 24 very large cavities. In 19 of these 64 patients either collapse treatment or resection was done after the cavities had closed; they were either patients seen early in the series before the risk of relapse after chemotherapy could be estimated or else they were thought to have a special risk of relapse.

*Bacteriological Results*

In 111 of the 142 patients *M. tuberculosis* was seen in smears or isolated on culture before treatment. The number of instances in which tubercle bacilli were either seen on direct examination of the sputum or grown on culture rapidly diminished during treatment. After three months' treatment they were found in 29 (26% of the original 111), after six months in 18 (16%), after nine months in only 9 (8%), after one year in 9, and subsequently in 6.

With 3 exceptions the isolation of *M. tuberculosis* after six months' treatment was always associated with easily demonstrable cavities (15 in 18).

After nine months' treatment 9 patients had *M. tuberculosis* on either smear or culture; all of them still had cavities which had been more than 3·5 cm. in diameter before treatment. However, not all the patients with persistent cavities continued necessarily to excrete tubercle bacilli: at nine months 13 still had cavities, but *M. tuberculosis* was isolated from only the 9 already mentioned, despite repeated attempts.

The susceptibility of *M. tuberculosis* to the drugs was tested in 8 of the 18 patients from whom tubercle bacilli were isolated at six months. From only 2 patients were tubercle bacilli found which were insusceptible to streptomycin: 1 of those patients deteriorated at this time and was given viomycin and treated surgically; the other continued to improve; and subsequently it was impossible to obtain *M. tuberculosis* from either of them.

*M. tuberculosis* was grown regularly from the sputum of 9 patients after a year's treatment; in 4 of them a few tubercle bacilli were found in sputum on direct examination. Subsequently the cavities of 4 of these patients were either removed or obliterated by surgery, and their sputum became sterile. Of the remaining 5 patients 3 continue to excrete *M. tuberculosis*, which can be grown on culture but is not present on direct smear. These are patients too old or too breathless for surgery in whom cavities are still present. Tubercle bacilli resistant to streptomycin and P.A.S. 5 μg. per ml. in the medium were found at some time in all 9 patients from whom *M. tuberculosis* was isolated after a year's treatment. Only 3 of these 9 patients produced tubercle bacilli insensitive to isoniazid 1 μg. per ml., and these 3 were the only ones of this group who had been given isoniazid for longer than the initial three months' treatment. In 2 other patients tubercle bacilli resistant to streptomycin but not to P.A.S. were isolated after six months' treatment. In 1 their presence coincided with radiographic and clinical deterioration. With this exception none of the patients in whom resistant tubercle bacilli were discovered has so far deteriorated from the state of maximal improvement earlier achieved. 6 have had chemotherapy for more than three years, and 2 for more than two years; the 9th died after a second operation designed to control an unclosed cavity and persistently positive sputum.

*Toxic Effects of Prolonged Chemotherapy*

Nausea ascribed to P.A.S. was common and was associated with persistent vomiting in 5 patients, diarrhœa in 3, and dyspepsia in 5. 2 patients developed these symptoms after a year's treatment, which was therefore stopped; 4 were given isoniazid instead of P.A.S.; and the others lost their symptoms after the dose of P.A.S. was reduced to 12 g. daily. 6 patients had pyrexia, a rash, and enlarged lymph-nodes due to either streptomycin or P.A.S.: desensitisation was successful in 4 but unsuccessful in the 2 others, who then continued their treatment with streptomycin and isoniazid. 7 patients had fairly severe aural disturbances. 3 became deaf from dihydrostreptomycin, 2 permanently; 3 had troublesome giddiness, 1 for a year after stopping the drug. All these 7 patients were aged more than 50 and were treated before the efficiency of combined treatment with isoniazid and P.A.S. was recognised; all were in class III. Since chemotherapy offered the sole means of arresting their tuberculosis, streptomycin was continued, but the dose was reduced to 2 g. a week. 7 patients had, within twelve hours of their injections, unpleasant reactions, including headaches, sweating, tremor, and persistent pain at the injection site. 2 were desensitised successfully; in the 5 others the symptoms were mild enough to be tolerated when streptomycin was given only twice weekly. 3 patients showed some enlargement of the thyroid gland caused by P.A.S., but no change in treatment was necessary.

### AFTER TREATMENT

*Present State of 142 Patients* (table VIII)

4 patients died: 1 from disseminated lupus erythematosus, which she had before chemotherapy was given; 1 after an operation for acute intestinal obstruction; and 2 from their tuberculosis (1 after thoracoplasty).

Of the remaining 138 none relapsed while under treatment. All became well and resumed work, usually soon after leaving the sanatorium and before completing their chemotherapy. 3 of them still have *M. tuberculosis* in their sputum; these patients had large cavities before treatment and are unsuited for surgical treatment. They are still under treatment by chemotherapy and so far have not relapsed.

2 patients have relapsed after stopping treatment: 1, a man with very extensive disease initially and pneumoconiosis, developed tuberculosis anew with a reopened cavity within a month after continuous chemotherapy for two years. Sensitive tubercle bacilli were found in his sputum. In the other, a woman with old tuberculosis in both lungs when first treated, a small cavity reopened, but she is well and symptomless.

In 134 patients either there is no sputum or what little there is does not contain *M. tuberculosis*. 126 are leading their ordinary lives with full activity, but 10 others are crippled to some extent by breathlessness, a legacy of extensive tuberculosis. 41 had either collapse treatment or resection as well as prolonged chemotherapy, comprising 8 of 23 in class I, 15 of 73 in class II, and 18 of 46 in class III. Prolonged chemotherapy alone was therefore successful in 101 of 142 patients, or roughly half of class III and three-quarters of classes I and II taken together.

TABLE VIII—FOLLOW-UP OF 142 PATIENTS AFTER PROLONGED CHEMOTHERAPY

| Class | No. of patients | No. of deaths | | Follow-up of 138 surviving patients | | | | | | Total more than 1 yr. |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Not due to tuberculosis | Due to tuberculosis | Up to 6 mos. | 6–9 mos. | 9 mos. to 1 yr. | 1–1½ yr. | 1½–2 yr. | More than 2 yr. | |
| I | 23 | 1 | — | 5 | 1 | 1 | 7 | 2 | 6 | 15 |
| II | 73 | 1 | — | 35 | 5 | 4 | 15 | 7 | 6 | 28 |
| III | 46 | — | 2 | 21 | 1 | 2 | 6 | 11 | 3 | 20 |
| Total | 142 | 2 | 2 | 61 | 7 | 7 | 28 | 20 | 15 | 63 |

*Duration of Observation after Treatment*

Up to June, 1955, 78 patients had been observed for six months or longer, and 63 for more than a year, after the completion of treatment. 2 relapsed as recorded above. All the others maintained their progress and are at work as at the end of treatment.

## Discussion

The value of antibacterial drugs in the treatment of pulmonary tuberculosis is now firmly established on evidence from therapeutic trials. These trials have been concerned mainly with short periods of treatment in patients with acute forms of the disease. They have not attempted to show for what length of time treatment may safely be continued, and they have not thrown any light on the optimal duration of treatment or on whether this may vary for different types of tuberculosis. On the answers to these questions, however, depends the most effective use of chemotherapy.

The rate of relapse was considerable among patients treated in the early trials of the Medical Research Council (Fox et al. 1954); and, although there were other reasons for this besides the short duration of treatment, the frequency of relapse has emphasised the need for longer treatment. Moreover relapses occur mainly within two years of apparent healing in most forms of pulmonary tuberculosis; hence treatment should be designed to protect the patient during this vulnerable time. A guide to the magnitude of the risk would be given by the rate of relapse among patients treated for a short period with combined chemotherapy as well as by conventional rest, sanatorium treatment, and such other measures as were thought to be necessary.

A. F. Foster-Carter (personal communication) has analysed the figures for patients at Frimley Sanatorium in 1950, a group comparable with the present series as regards age, sex, and social background. The extent of disease and the proportion with cavities were also similar. Of his 90 patients 81 had chemotherapy for three months or less and the remainder for four to six months. All of them had routine rest in bed followed by graded exercise, and in addition 61 had other forms of treatment: 52 collapse treatment of some kind, including 8 treated surgically; and a further 9 resection. Of these 90 patients 1 died, 7 relapsed within a year of leaving the sanatorium, and 4 others relapsed in the following two years—a total relapse-rate of 12% in three years from the completion of treatment. These figures show that there is still a significant rate of relapse when present resources are used, including chemotherapy for short periods. It is therefore important to know whether prolonged chemotherapy is more effective, and to what extent it can either supersede or supplement either collapse treatment or resection.

During the past five years we have used prolonged chemotherapy as a routine, combining it when necessary with either collapse treatment or resection (41 in 142). All the patients were rested in bed, and subsequently their activity was gradually increased. In 101 prolonged chemotherapy was the only additional treatment. Our experience is that the use of antibacterial drugs in this way is practicable and safe.

119 patients were treated continuously for more than a year, 12 of them for more than two years. Minor symptoms, nausea especially, were common although they were rarely persistent and could usually be overcome. Vertigo in older patients and reactions caused by drug sensitivity were more important, but severe disturbance was exceptional. Such symptoms were usually got rid of by changing the drugs or by desensitisation. Only 3 patients were left with a disability from chemotherapy: deafness in 2 from dihydrostreptomycin and vertigo in 1 from streptomycin. These 3 patients were treated at a time when isoniazid was not available. It is evident that the risk of serious toxicity is slight and does not increase materially with the length of time for which antibacterial drugs are given.

The immediate effects of prolonged treatment were shown by the length of time for which the tuberculous lesions continued to resolve and heal, and by the frequency with which cavities were closed and sputum was converted. In 73 of the 142 patients radiographic improvement continued during treatment for more than six months and in 24 of these for a year or longer (table VI). The period of improvement increased with the extent of disease: a third of the patients in class I, half of those in class II, and two-thirds of those in class III improved radiographically for more than six months. 11 of 46 patients in class III improved for a year or longer. These results show that tuberculosis often improves radiographically when chemotherapy is continued well beyond the usual time, and that patients with advanced tuberculosis benefit especially.

Cavities were closed by rest and prolonged chemotherapy alone in 64 of 92 patients (69·5%). The proportion was greatest for small or medium cavities (23 in 27 and 21 in 25 respectively) but considerable even for large and very large ones (9 in 16 and 11 in 24 respectively). Most cavities were obliterated during the first six months' treatment, though a few large and very large cavities (6 in 20) did not close until later (table VII). As expected, the age of cavities and fibrosis around them appeared to affect the chances of closure by chemotherapy; in the present series most of the cavities which did not close had been present for several years and were situated in the midst of dense shadows which were unaltered by the drugs. Another less common type of cavity seen in isolated solid lesions (3 in this series) also did not respond to chemotherapy alone. Those cavities which had not closed after six months' chemotherapy often required either collapse treatment or resection. It is, however, worth emphasising that, if surgery is impossible, further chemotherapy may still be successful.

The closure of cavities is an important factor in deciding the bacteriology of the sputum during prolonged chemotherapy. The sputum was converted in three months in 74% of 111 patients with *M. tuberculosis* present initially, in six months in 84%, and in nine months in 92%. After six months' treatment the presence of *M. tuberculosis* in the sputum was almost always associated with obvious cavities in the lung (in 15 of 18). The risk that such cavities may not be closed by chemotherapy alone has already been emphasised. After nine months' treatment the few patients with *M. tuberculosis* still present usually retained them, unless the cavities could be dealt with surgically; moreover the tubercle bacilli were usually insusceptible to the drugs. However, sputum from 4 of 13 patients who had persistent cavities after nine months' treatment did not grow *M. tuberculosis* despite repeated attempts.

There were 2 deaths from tuberculosis and 2 not caused by tuberculosis. Both patients who died from tuberculosis had extensive lesions; 1 of them died soon after a thoracoplasty. 10 patients are respiratory cripples, and 2 others have relapsed: all but 1 of these had very advanced tuberculosis before treatment. The remaining 126 patients are at present well and at work, and lead their ordinary lives. Most of them resumed work some time before their chemotherapy was stopped. In 134 of the 138 survivors either there is no sputum or the little remaining sputum is free from *M. tuberculosis*. 101 were treated with prolonged chemotherapy alone: about three-quarters of those in classes I and II and half of those in class III. The results at a year or longer from the termination of treatment confirm these favourable figures: 61 of 63 patients remain well and show no evidence of relapse.

These results of prolonged chemotherapy make it a direct competitor with treatment by surgical resection of a lobe or a segment when the tuberculosis is localised (classes I and II), especially since the mortality among patients treated by chemotherapy is insignificant. In a preliminary report on the recent national survey (British Tuberculosis Association 1955) the mortality among 3183 patients was 1·3% for segmental resection, 2% for thoracoplasty, and twice this figure for lobectomy. Contralateral spread of disease occurred in 2·9% after thoracoplasty, and in 2·4% after lobectomy; and 4% of resections were followed by a bronchopleural fistula. It therefore seems that prolonged chemotherapy is the treatment of choice for most patients. A minority of those with localised tuberculosis in whom this fails or who subsequently relapse require either collapse treatment or resection. In this way the risk of complications which arise from surgical treatment can be confined to those few patients for whom such treatment is essential after the failure of chemotherapy.

Patients with recent and very extensive tuberculosis unsuitable for surgical treatment can sometimes be brought to a state of fitness for surgery by prolonged chemotherapy when this controls disease outside the field of operation. In our experience it is impossible at the outset to estimate the enormous improvement which such patients may show after chemotherapy for nine months or longer.

The main limitation of prolonged chemotherapy is in patients with fibrotic tuberculous lesions and large cavities who are too old or too breathless ever to be likely to be fit for surgery. Indeed it may be doubted whether antibacterial drugs should be used for this kind of tuberculosis, because of the risk that eventually sputum may persist containing bacilli resistant to the drugs. Patients who are temperamentally unstable and incapable of education in the care of sputum (they are very few) must be regarded as unsuitable because of the danger to those in contact with them. But experience with the present series shows that, though resistant tubercle bacilli have developed in about the same proportion of patients as in the series reported by the Medical Research Council, except for 1 patient there has been no corresponding halt to clinical or radiographic progress. The explanation for this as Mitchison (1954) has emphasised, is that the tubercle bacilli resistant to streptomycin in a given sputum specimen are different ones from those resistant to isoniazid or to P.A.S. Thus, if the drugs are combined and given continuously, neither resistant strain can flourish, and the mathematical chances of mutations arising in such a way as to produce tubercle bacilli resistant to two drugs are very small indeed. This agrees with our experience and minimises the significance of the appearance of tubercle bacilli resistant to single drugs.

The results in the present series show that there are many patients with extensive fibrotic cavitated tuberculosis and illness of long duration to whom prolonged chemotherapy restores the ability to live useful and satisfactory lives. Moreover the arrest of much active tuberculosis and the improvement in health which follows may still allow either surgical collapse or resection of cavitated lung when the cavities have not closed. In the present series there were 9 such patients in whom an apparently hopeless situation was improved to a point where surgery could complete the process of sputum conversion and cavity closure.

Finally, it should be emphasised that, although the period of drug treatment is long, most patients return to work during this time, and the length of time spent in hospital and sanatorium is no longer than with other methods of treatment. Indeed one question for the future, especially for some limited forms of the disease, is whether the period of rest can be very considerably reduced when prolonged chemotherapy is undertaken.

### Conclusions

Prolonged chemotherapy for pulmonary tuberculosis is practicable and safe.

142 patients were treated by chemotherapy for nine months or more, 119 of them for a year or more.

134 are well, their cavities are closed, and *M. tuberculosis* cannot be recovered from them; 126 of these are leading normal lives, but 10 are restricted by breathlessness.

These results were achieved solely by chemotherapy and rest in 101 patients; 41 other patients required surgery or other collapse measures in addition.

92 patients had cavities; in 64 the cavities were closed without the aid of surgery or collapse treatment.

63 patients have been followed for a year after the end of chemotherapy; only 2 relapsed.

Radiographic clearing was still taking place between the sixth and ninth month of treatment in 51%, and up to a year in 14%.

Cavities not closed within six months are less likely to close subsequently on chemotherapy alone and are often associated with resistant *M. tuberculosis* in the sputum. They require either surgical resection or collapse treatment when possible in addition to further chemotherapy.

Prolonged chemotherapy is often an effective treatment for advanced chronic tuberculosis or may make possible otherwise impracticable surgical treatment.

We are much indebted to Dr. A. F. Foster-Carter for the analysis of the results at Frimley Sanatorium, and to the medical committee of Brompton Hospital for permission to quote them. One of us (J. D.) was in receipt of a personal grant from the research fund of Brompton Hospital.

REFERENCES

British Tuberculosis Association (1955) Annual general meeting, June. National Survey by British Tuberculosis Association and Society of Thoracic Surgeons. See *Lancet*, 1955, ii, 83.

Foster-Carter, A. F., Myers, M., Goddard, D. L. H., Young, F. H., Benjamin, B. (1952) *Brompton Hosp. Rep.* **21**, 1.

Fox, W., Sutherland, I., Daniels, M. (1954) *Quart. J. Med.* **23**, 347.

Mitchison, D. A. (1954) *Brit. med. Bull.* **10**, 115.

## A DUODENAL-ULCER FAMILY

J. T. WRIGHT
D.M. Oxfd, M.R.C.P.
SENIOR ASSISTANT, MEDICAL UNIT

ALAN GRANT
M.D. Aberd., M.R.C.P.
LECTURER IN FORENSIC MEDICINE

DENYS JENNINGS
B.M. Oxfd, D.M.R.E.
RESEARCH FELLOW IN GASTRO-ENTEROLOGY

THE LONDON HOSPITAL

MANY "ulcer families" have been described since the beginning of the century. All members of the family described here have been personally investigated, and we have listened to brothers and sisters arguing among themselves as to why some of them have escaped having ulcers. 2 patients had operations at other hospitals and the surgeons concerned kindly wrote to confirm the diagnosis.

Aird et al. (1953, 1954) have shown that patients with group-O blood are more liable to peptic ulcer than those of group A, who are more liable to gastric carcinoma. There is evidence (Clarke 1955, Westlund and Heistö 1955) that the increased liability of group-O patients applies to duodenal and not to gastric ulcers, and Køster et al. (1955) have shown that group O is associated with higher gastric acidity than group A.

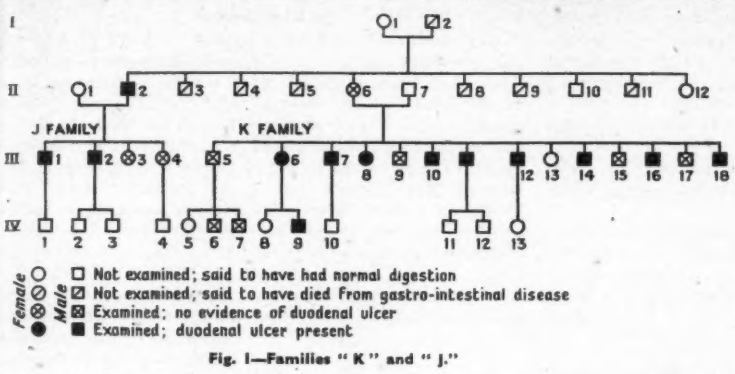



Fig. 1—Families "K" and "J."

## Family History

The two branches of the family (fig. 1) are first cousins. The "K" branch presumably inherited its ulcer tendency through the mother (II.6). The father (II.7) had a good digestion; he died from influenza in the 1918 epidemic. The mother has also always had a good digestion. She does not remember her own mother (I.1) complaining of indigestion; but her father (I.2) died from "abdominal trouble" at the age of 46, and only 1 of her 8 brothers is completely free from the suspicion of gastro-intestinal disease. The eldest brother (II.2) had a gastro-enterostomy at the London Hospital in 1912; his 4 children are the "J" family. As regards the others, II.3 had an operation for ulcer; II.4 and 8 are said to have had cancer of the stomach (? pyloric stenosis); II.9 and II.11 had "trouble with the gullet"; and II.5 had cancer of the throat. The only sister (II.12) had a normal digestion.

Apart from a tendency to contract duodenal ulcer, the "K" family is healthy. The mother married in 1893 at the age of 19, came from Cornwall to London in 1898, and has since lived in the East End. Between 1895 and 1917 she had 14 children and 2 miscarriages. All the children except III.13, who died from influenza at the age of 7, are still living; 7 had "pneumonia" but were otherwise healthy, and nothing in childhood explains what happened later. They all left school at the age of 14, and with the exception of III.8 and III.14 went to work in a local sugar refinery. Their subsequent occupations differ, but all except III.12, who was in a reserved occupation, served in the 1914–18 or 1939–45 war. Their statures are slight—only III.11 and III.18 ever exceeded 10 st. in weight—but they have been interested in sport, and several have excelled at soccer and cricket. There is some slight tendency to sciatica and hæmorrhoids, and III.11 was investigated in 1942 for an upper-motor-neurone lesion; this has got no worse and he still does a full day's manual work.

32 members of the fourth generation are living but only those over the age of 20 are shown in fig. 1. Of the 2 patients over 30, 1 (IV.6) has had discomfort for many

TABLE I—DETAILS OF "K" AND "J" FAMILIES

| Place in family | Sex | Year of birth | Age at marriage (yr.) | No. of children | Alcohol | Tobacco | Age (yr.) at which dentures fitted | X-ray findings*† | Comment |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | THE "J" FAMILY | | | |
| II.2 | M | 1858 | ? | 4 | ? | ? | 54 | .. | Onset of indigestion as seaman aged 34. Gastro-enterostomy for ? gastric ulcer aged 54 |
| III.1 | M | 1900 | 25 | 1 | ++ | + | 53 | + | Onset of symptoms aged 30, two years after getting naval commission. Partial gastrectomy aged 49 |
| III.2 | M | 1902 | 25 | 2 | + | + | 46 | + | Frequent mild attacks of indigestion since age of 25. Clerical work except for 1939–45 (Army sergeant) |
| III.3 | F | 1906 | Single | .. | ± | − | .. | − | No indigestion apart from "waterbrash" and discomfort at age 18–21, soon after starting work as typist |
| III.4 | F | 1913 | 23 | 3 | ± | − | .. | − | Frequent bilious attacks since appendix abscess in childhood. More prolonged indigestion since 1954. Housewife |
| | | | | | | THE "K" FAMILY | | | |
| II.6 | F | 1874 | 19 | 14 | − | − | .. | .. | No indigestion. Housewife |
| III.5 | M | 1895 | 25 | 3 | ++ | ++ | 28 | ± | Indigestion while in the trenches in France, aged 21. First bad attack in 1919–20 after return to the sugar refinery |
| III.6 | F | 1898 | 24 | 2 | − | − | 42 | + | Severe attacks of diarrhœa and vomiting as a child. Indigestion since 16, when she changed from sugar refinery to rubber factory |
| III.7 | M | 1899 | 28 | 2 | ± | ++ | 53 | + | Onset of symptoms at 21 soon after demobilisation and return to sugar refinery |
| III.8 | F | 1900 | Single | .. | ± | − | 53 | + | Bad attack of indigestion in 1940 when a municipal employee. Only mild attacks since |
| III.9 | M | 1902 | 32 | 4 | ± | + | 52 | ± | Mild attacks of indigestion at age 33–37 while working in paper mill. No trouble in the Army (1940–45), or since going back to paper mill |
| III.10 | M | 1903 | 31 | 1 | ± | + | 31 | + | Indigestion for most of working life (sugar refinery). First bad attack at 50 |
| III.11 | M | 1904 | 25 | 4 | + | + | 24 | + | Indigestion since marriage at 25. First bad attack 5 years later in 1934. Work in sugar refinery, except for war service in the Pioneer Corps |
| III.12 | M | 1907 | 23 | 2 | ± | + | 33 | + | Onset of symptoms at 21 after breaking jaw and transferring from sugar refinery to aluminium works. Partial gastrectomy in 1949 |
| III.14 | M | 1911 | 35 | 2 | ± | + | .. | + | Mild attacks of indigestion since 1944. Clerical work all life, except 1940–45 (R.A.F. drill instructor) |
| III.15 | M | 1912 | 30 | 1 | + | ++ | 34 | − | Never any indigestion. Sugar-refinery work all his life except for 1940–46 (Army P.T. instructor) |
| III.16 | M | 1913 | 35 | 1 | ++ | + | .. | + | First attack of indigestion in 1952 at 39. Garage work since 1948 (previously Royal Navy) |
| III.17 | M | 1914 | 36 | 2 | ++ | ++ | .. | − | Gingivitis followed by bad indigestion in 1946 while on the Control Commission in Germany. Suspected carcinoma of the stomach; little trouble since. Army since age 19 |
| III.18 | M | 1917 | 25 | 1 | − | + | .. | + | First attack of indigestion at 36 soon after becoming insurance agent. Previously at sugar refinery, except 1941–46 (R.A.F. ground crew) |
| IV.9 | M | 1930 | Single | .. | − | + | .. | + | Onset of symptoms at 15. Discharged from army in 1948 after 14 days' service. No settled work |

* Refer to duodenal cap only. † Under X-ray findings, + = definite evidence of ulcer; ± = doubtful ulcer; − = no evidence of ulcer.

years; but his stomach and duodenum appeared normal on radiography, and the discomfort probably originates in the colon. 1 (IV.9) of the 11 aged 20–29 has ulcer symptoms; these started at the age of 15, and now at the age of 25 his duodenum is badly scarred.

Further details about both branches of the family are given in table I.

Fig. 2 shows tracings from the radiographs; no radiographs were available for patients III.1 and III.12, who were operated on at other hospitals.

Table II shows the blood-groups and the threshold of taste to phenylthiourea (P.T.C.). The method of Harris and Kalmus (1949) was used, and those patients unable to taste concentrations weaker than 81·25 mg. per litre are termed "non-tasters."

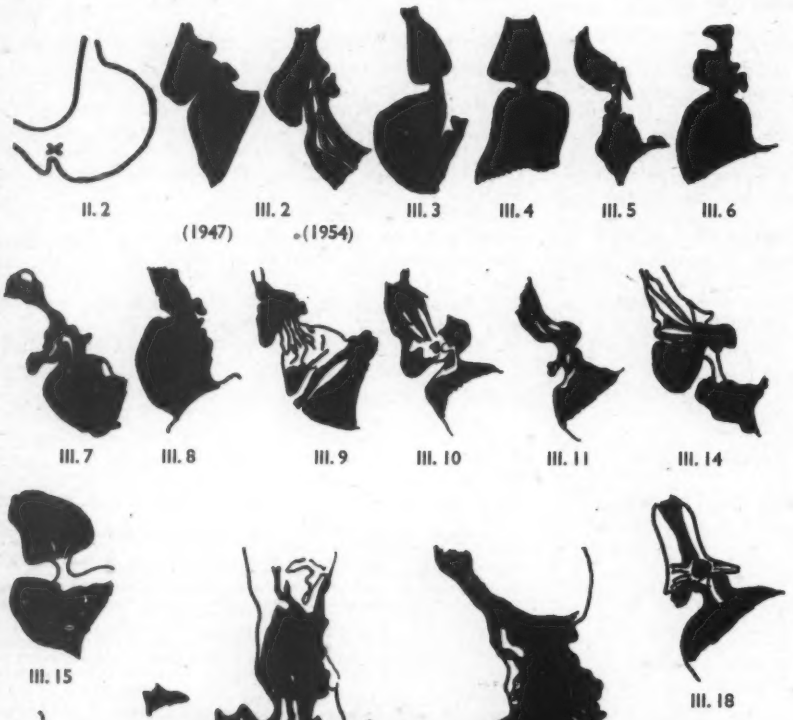



**Fig. 2—Tracings of radiographs in families "K" and "J."**

II.2: Tracing of operation sketch in 1912. X = site of ulcer.
III.2 (1947 and 1954): "saddleback" scar. Note similar deformity in cousins III.6 and III.8.
III.3: Normal duodenal cap.
III.4: Normal duodenal cap.
III.5: Doubtful deformity.
III.6: "Saddleback" ulcer or scar.
III.7: Considerable scarring with posterior-wall crater.
III.8: "Saddleback" scar. Deformity of medial basal angle as in patient III.6.
III.9: Pyloric prolapse. Minimal "hour-glass" deformity.
III.10: Little distortion but definite ulcer crater.
III.11: Considerable scarring. Dubious ulcer crater.
III.14: "Saddleback" crater.
III.15: Slight pyloric prolapse.
III.16: Minimal deformity. The posterior-wall crater was constant in all serial films.
III.17: (1946 and 1954). "Giant" gastritis. Normal duodenal cap.
III.18: Considerable scarring and ulcer crater.
IV.9: Considerable scarring.

## Discussion

Doll and Kellock (1951) appear to have proved that the tendency to contract duodenal ulcers is inherited. There has been a considerable increase in the incidence of duodenal ulcers during this century; and unless harmful genes have accumulated at an improbable rate the cause must be something harmful in the environment. If this is so, it would be very surprising if some genetic strains were not more sensitive than others (Jennings 1940). The sensitivity of animals to poisons or deficient diets varies, and by inbreeding it is possible to produce strains of high and low sensitivity (see Russell 1955).

It is interesting that one generation of this family was so severely affected. It is difficult to be sure how many members of the preceding generation had duodenal ulcers, but the fourth generation seems so far to be relatively immune. If we assume that all members of the "K" branch had an increased susceptibility to duodenal ulcers, differences in their backgrounds might explain why some have had more trouble than others. In fact, no such explanation emerged. They were all brought up under conditions of hardship and financial stress, and routine inquiries into possibly harmful stresses gave negative results.

### *Sugar and Dental Decay*

There is evidence (Harris 1935) that excess sugar predisposes to instability of the autonomic nervous system, and many persons have less indigestion or are cured by a sugar-free diet. But sugar does not appear to be an important factor in this family, because patients III.8 and 14, the only 2 members of the family who never worked in the sugar refinery, have ulcers. Only 1 brother (III.15) attributed early dental decay to his easy access to sugar but he did not develop an ulcer, whereas the members of the family with ulcers usually retained their teeth until long after the onset of symptoms. 1 exception, patient III.5, had indigestion from 1916 to 1920 and lost all his teeth in 1923. He never wore dentures for eating, but had little trouble in the next thirty years and now has only a minimal deformity of the duodenal cap.

### *Tobacco and Alcohol*

All the men of the "K" branch have smoked

TABLE II—BLOOD-GROUPS AND TASTE SENSATIONS TO PHENYLTHIOUREA

| Place in family | Blood-groups | | | | | | | | Blood-antigen in saliva | Phenylthiourea taste threshold | | Duodenal ulcer |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | ABO | MNS | P | Rhesus | Kell | a Duffy | a Lutheran | a Lewis | | Conc. (mg. per litre) | Interpretation | |
| III.1 | B | .. | .. | CDe/cde | .. | .. | .. | .. | .. | .. | .. | + |
| III.2 | B | MN.S | − | CDe/cde | − | − | − | + | ns | 650 | nt | + |
| III.3 | B | MN.S | − | CDe/cde | − | + | − | − | s | <81·25 | T | − |
| III.4 | O | MN.S | − | cde/cde | − | + | − | − | s | >81·25 | nt | − |
| II.6 | O | NsNs | − | cde/cde | − | − | − | − | s | 325 | nt | − |
| III.5 | O | MN.S | + | cde/cde | − | − | − | + | ns | >1300 | nt | ± |
| III.6 | O | NsNs | − | cDE/cde | − | − | − | − | s | >1300 | nt | + |
| III.7 | O | NsNs | − | cDE/cde | − | + | − | + | ns | 1300 | nt | + |
| III.8 | O | MN.S | + | cDE/cde | − | − | − | − | s | 650 | nt | + |
| III.9 | O | MN.S | + | cde/cde | − | + | − | + | ns | >1300 | nt | ± |
| III.10 | O | MN.S | − | cDE/cde | − | − | − | + | ns | 1300 | nt | + |
| III.11 | O | NsNs | − | cDE/cde | − | + | − | − | s | >1300 | nt | + |
| III.12 | O | NsNs | + | cDE/cde | − | + | − | + | ns | 1300 | nt | + |
| III.14 | O | MN.S | − | cDE/cde | − | + | − | − | s | 20·31 | T | + |
| III.15 | O | MN.S | + | cde/cde | − | − | − | − | s | 650 | nt | − |
| III.16 | O | MN.S | − | cDE/cde | − | − | − | − | s | 1300 | nt | + |
| III.17 | O | MN.S | + | cDE/cde | − | − | − | − | s | 5·08 | T | − |
| III.18 | O | NsNs | + | cde/cde | − | + | − | − | s | 81·25 | T | + |
| IV.9 | O | .. | .. | .. | .. | .. | .. | .. | .. | 1300 | nt | + |

T = "taster"; nt = "non-taster"; s = secretor; ns = non-secretor.

heavily, but the 2 without ulcers are said to have smoked even more heavily, and the 2 sisters with ulcers have never smoked. On the other hand, patient III.7 stopped smoking in 1951 and has since had no serious indigestion, and patient III.12 who stopped smoking from 1944 to 1945 was considerably improved.

5 brothers admitted to fairly heavy alcohol consumption at one time or another. 2 of them (III.11 and 16) have ulcers, and 2 (III.15 and 17) have not. The 5th (III.5) may have had an ulcer; he has had mild symptoms and his radiographs are not completely normal.

The "mystery" stomach in the family is that of patient III.17 (fig. 2). The diagnosis of "giant" gastritis is made by one of us (D. J.) in fewer than 1 in 2000 barium-meal examinations and this was a particularly good example. His symptoms, followed a period of severe oral sepsis with overindulgence in both alcohol and tobacco. In 1946 and 1954 the duodenal cap was radiographically normal.

Nothing is known about the ætiology of "giant" gastritis. Spriggs (1943) mentions alcohol and sepsis, but there is much doubt as to whether there is such a disease as chronic alcoholic gastritis (Palmer 1954).

*Social and Psychological Factors*

It is fashionable to link duodenal ulcers with deep-seated emotions. These are influenced by place in the family. Kellock (1951) showed, however, that place in the family had no detectable influence on ulcer incidence. Age at marriage and number of children must also be linked with character, but the relation to indigestion is complicated. Indigestion is sometimes given as a reason for marriage; the patient feels that it is time he settled down. Others insist that their symptoms started soon after marriage or after setting up a home. In this family, the onset of symptoms seems to be only loosely linked with marriage. In patients III.5, 12, and 14 symptoms started three to four years before marriage, and in patients III.9 and 16 within four years after marriage; and only in patient III.11 did the first attack of indigestion occur in the year of marriage.

In some of those affected (III.5, 6, 7, 12, and 18) ulcer symptoms appear to be related to change in occupation. As in the case of marriage, it is difficult to distinguish between cause and effect, but in those patients (III.5 and 7) where change of occupation was presumably obligatory, this was possibly a factor.

No deep search was made for psychological causes. With the exception of 1 member of the fourth generation (patient IV.9) who is mildly psychopathic, the family gives the impression of being essentially normal.

The "J" family was smaller and their upbringing was different, but nevertheless the 2 men in generation III both have ulcers and the 2 women, despite negative radiographic findings, have had suspicious symptoms. Their mother (II.1) was apparently unaffected, but their father (II.2) is said to have had a "gastric" ulcer, although there is some doubt about this. The operation sketch (fig. 2) shows the ulcer near the pylorus, but mistakes in localising pyloric ulcers have always been common.

*Radiography*

The radiographic appearance of the gut, particularly the outline of the stomach and the splenic flexure of the colon, was much the same in all the "K" siblings. The shape of the duodenal cap varied widely, but in 2 sisters (III.6 and 8) there was an identical hook-like projection at the base of the cap on the side of the lesser curve, and 2 of the men (III.5 and his cousin III.2) had a lesser degree of the same deformity (fig. 2).

In several cases it was impossible to get good films because the duodenal loop was relatively small, and the third part of the duodenum which lay behind the cap, tended to remain filled with barium.

*Blood-groups and Taste Sensation*

The blood-group results are ambiguous. All members of the "K" family whether they have an ulcer or not are group O, but the cousins III.1 and III.2 who have ulcers are group B (table II). The subsidiary blood-groups and ability to secrete blood-group antigens in the saliva are not correlated with the presence or absence of ulcers. We used the relationship between the presence in the blood of the Lewis antigen and failure to secrete blood-antigen to confirm whether group-O patients were "secretors" or "non-secretors."

Taste-testing with P.T.C. showed that, although about two-thirds of healthy people are "tasters," 10 out of 13 of the "K" siblings were "non-tasters," and the only unequivocal "taster" (patient III.17) had a normal duodenum.

## Summary

A family ("K") is described in which 9 out of 13 living siblings have duodenal ulcers. In 2 there was some evidence of past ulceration, and in only 2 was the duodenal cap radiographically normal; 1 of these 2 had "giant" gastritis. Of 4 cousins (the "J" family) 2 have duodenal ulcers.

There is no evidence that psychological factors or anything in the mode of life determined which members of the family developed ulcers.

All members of the "K" family belong to blood-group O. 2 affected members of the "J" family belong

to group B. Nearly all the members of the "K" family are "non-tasters" of phenylthiourea, and the only member who is an unequivocal "taster" has no duodenal ulcer.

We thank Mr. D. M. Cooper and Mr. J. D. Younghusband for the operation reports of patients III.12 and III.1, and Prof. Clifford Wilson and Dr. H. Harris for advice. We are grateful to the family for their willing coöperation.

REFERENCES

Aird, I., Bentall, H. H., Mehigan, J. A., Roberts, J. A. F. (1954) *Brit. med. J.* i, 799.
— — Roberts, J. A. F. (1953) *Ibid*, ii, 315.
Clarke, C. A. (1955) *Lancet*, i, 544.
Doll, R., Kellock, T. D. (1951) *Ann. Eugen., Lond.* **16**, 231.
Harris, H. R., Kalmus, H. (1949) *Ibid* **15**, 24.
Harris, S. (1935) *Amer. J. dig. Dis.* **2**, 557.
Jennings, D. (1940) *Lancet*, i, 395.
Kellock, T. D. (1951) *Brit. med. J.* ii, 1117.
Køster, K. H., Sindrup, E., Seele, V. (1955) *Lancet*, ii, 52.
Palmer, E. D. (1954) *Medicine, Baltimore*, **33**, 199.
Russell, E. S. (1955) *Brit. med. J.* i, 826.
Spriggs, E. I. (1943) *Quart. J. Med.* **36**, 1.
Westlund, K., Heistö, H. (1955) *Brit. med. J.* i, 847.

# THALASSÆMIA IN A SCOTTISH FAMILY

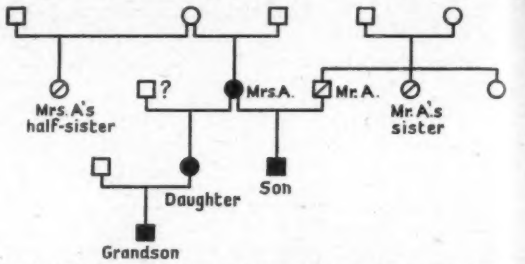
LYONEL G. ISRAELS
M.D., M.Sc. Manitoba, F.R.C.P.(C.)
ASSISTANT PROFESSOR OF BIOCHEMISTRY, UNIVERSITY OF MANITOBA

HAROLD J. SUDERMAN
M.Sc. Manitoba
LECTURER, DEPARTMENT OF BIOCHEMISTRY, UNIVERSITY OF MANITOBA

JAN HOOGSTRATEN
M.D., Ph.D. Camb.
PATHOLOGIST, GRACE HOSPITAL, WINNIPEG

IN 1925, Cooley and Lee described an anæmia in children characterised by jaundice, splenomegaly, a "peculiar mongoloid appearance," reticulocytosis, and normoblasts in the peripheral blood. Additional features of the disease were radiographic signs of skeletal changes and decreased erythrocyte osmotic fragility. Then, 2 years later, they reported with Witwer seven cases of which two patients were Italian, one Greek, one Syrian, one Mulatto, and one English (Cooley et al. 1927). The last two were later withdrawn from the series (Cooley and Lee 1932). The disease was subsequently reported in Italians, Greeks, Armenians, and Syrians. The striking geographical incidence was responsible for the name "Mediterranean anæmia" or thalassæmia which was given to this hæmolytic anæmia (Whipple and Bradford 1932). But as the hereditary pattern of the disease became known and milder forms were recognised, it became increasingly evident that it was not limited to people of Mediterranean extraction.

Evidence rapidly accumulated that this disease is widely distributed geographically, and that many ethnic groups are affected though it is, of course, difficult to rule out any remote Mediterranean ancestry. Thalassæmia has been reported in those of Turkish descent (Saracoglu 1943), in Chinese and Mexicans (Silver 1950), in Egyptians (Diwani 1944), amongst Bucharan and Kurdistan Jews (Schieber 1945, Matoth et al. 1955), in Negroes (Schwartz and Mason 1949), as well as in patients from India (Dhayagude 1944), Thailand (Minnich et al. 1954), and possibly in an American Indian (Prouty 1950). Included in the few cases which have been found amongst Northern Europeans are two children probably of German stock (Freudenberg and Esser 1942), a 10-year-old English girl reported by Bywaters (1938), and a 9-year-old boy of Anglo-Irish parentage by Grinnan (1935), although little evidence was given in this case to support the diagnosis. Cooley et al. (1927) recorded the disease in an English girl aged 3, but this case was later removed from the series. Because of the rarity of this type of hæmolytic anæmia in the British Isles, we record the occurrence of thalassæmia in a Scottish family.




**The A family. A solid square indicates an affected male, a solid circle an affected female. The symbols crossed by diagonal lines are members of the family found to be normal, while the members represented by open symbols were not examined.**

The accompanying figure indicates the pattern of inheritance in this family. Both parents (Mr. and Mrs. A) were born in Scotland, in Dundee, and none of their ancestors are known to have originated outside Scotland. The paternity of the daughter is uncertain. Although acknowledged as the child of Mr. and Mrs. A, Rh blood-grouping showed that it was impossible for Mr. A. to be her father. This is additional evidence that the pattern of inheritance is through Mrs. A to both children and her grandson.

## Case-reports

*Normal Members of the Family*

*Mr. A.*—Blood-groups: $A_1$; M+, N+; P+; C+, C$^w$–, c–, D+, E–; K–; Le(a–); Fy(a–). Aged 53. Born in Dundee, as were both his parents who still live there. He has had no serious illnesses, and has been well all his life. No physical abnormalities were found, and the results of laboratory investigations were normal.

*Mr. A's sister.*—Blood-groups: $A_1$; M+, N–; P+; C–, C$^w$–, c+, D+, E–; K–; Le(a–); Fy(a–). Aged 55. A healthy woman with no physical abnormalities.

*Mrs. A's half-sister.*—Aged 38. There were no abnormal physical or hæmatological findings.

*Affected Members of the Family*

*Mrs. A.*—Blood-groups: $A_1$; M+, N+, P+; C–, C$^w$–, c+, D+, E+, e+; K–; Le(a+); Fy(a+). Aged 55. Born in Dundee, as were both her parents. She had been both "anæmic" and "jaundiced" since childhood, but had received no treatment. She knew of no-one else in the family other than her children who was similarly affected. Her father had died at 60 of carcinoma of the stomach, her mother at 73 of diabetes mellitus. She was a middle-aged woman with slight jaundice of the skin and scleræ. She had a mongoloid appearance, with epicanthic folds. Her spleen was palpable 4 cm. below the left costal margin, and the liver 2 cm. below the right costal margin.

*The son.*—Blood-groups: $A_1$; M+, N+; P+, C+, c+, D+, E+, e+; K–; Le(a+); Fy(a+). Aged 14. He was taken to a doctor at the age of 6 because of jaundice, and was found to have anæmia and a large spleen. His jaundice persisted and became severe on occasions. Iron and liver therapy was given without effect, and in August, 1953, he was admitted to hospital for splenectomy. The only abnormal findings were jaundice, and a spleen palpable 4 cm. below the left costal margin. The accompanying table shows the pre-operative laboratory findings.

The spleen weighed 363 g. and measured 15 × 10 × 6 cm. The cut surface was a normal dark red and not abnormally soft or pulpy. The malpighian bodies and fibrous trabeculæ were normal and so was the general anatomy of the spleen and its cell population. No hyperplasia of the reticulum or hæmopoiesis were evident, and no erythrophagocytosis was seen. The supporting and littoral cells contained a moderate amount of hæmosiderin.

Splenectomy had little effect on the anæmia or the jaundice, and he was again admitted to hospital in October, 1954, for blood-transfusion. It was then that we first saw him. He was an intelligent boy who did well at school and, despite his anæmia, led a fairly normal life. He was heavily freckled, and his skin had a yellow pallor. The bridge of his nose was flat;

there were striking epicanthic folds, and puffiness under his eyes. The hæmatological findings are in the table, which shows an increase in the number of circulating normoblasts in the peripheral blood following splenectomy. There was considerable normoblastic hyperplasia of the bone-marrow. Radiography of the skull and hands showed no abnormalities. The red cells did not "sickle" in a sodium metabisulphite preparation.

*The daughter.*—Blood-groups: $A_1$; M+, N+; P+; C–, $C^w$–, c+, D+, E–; K–; Le(a+); Fy(a+). Aged 25. She had had jaundice, and anæmia for which she had received various hæmatinics with no benefit, "since birth." Her jaundice became intense during her pregnancy in 1953, and she was admitted to hospital where she was found to have an icterus index of 100, a red blood-count of 2·4 million per c.mm., of which 12% were reticulocytes; there were 14 normoblasts per 100 white cells. Numerous target-cells were seen in the smear. She received six pints of blood, and was delivered of a full-term infant 2 months later. When seen by one of us in October, 1954, she bore a striking resemblance to her mother and brother. She was slightly jaundiced, and the epicanthic folds and the puffiness beneath the eyes gave her a mongoloid appearance. Her spleen was palpable 2 cm. below the left costal margin. A sodium-metabisulphite sickle-cell test was negative.

*The grandson.*—Aged 2. An apparently healthy child who has had no serious illnesses. He resembled the other members of the family in his mongoloid appearance and epicanthic folds, but he was not jaundiced. His spleen was not palpable.

## Hæmoglobin Investigations

The hæmoglobin of members of the family was examined with respect to alkali resistance, electrophoretic mobility, and solubility. Parallel tests were done on normal adult and umbilical-cord blood.

*Alkali-resistant Hæmoglobin (Hæmoglobin F or Fœtal Hæmoglobin)*

This was measured both by the method of White et al. (1950) and by the method of Singer et al. (1951). The two methods gave almost identical values; the results of the latter method are given in the table. The normal adult value for hæmoglobin F is under 2%, and results for all the normal members of the family were below this figure. The affected members had hæmoglobin-F levels of 11%, 12%, and 18%.

*Electrophoretic Mobility*

Solutions of hæmoglobin suitable for paper electrophoresis were prepared from citrated blood. Red cells were washed three times with 0·9% saline, and hæmolysed by shaking with an equal volume of distilled water and 0·4 volume of toluene. After centrifuging, the concentrations of the clear hæmoglobin solutions determined by spectrophotometry, varied from 11 to 14 g. per 100 ml.

A Shandon vertical paper electrophoresis apparatus was used. Strips of Whatman no. 1 filter-paper, 36 × 5 cm., were suspended in the tank and allowed to moisten by capillary action for 2 hours in a veronal buffer of pH 8·6. Two µl. each of the test sample, normal adult, and cord-blood hæmoglobin solutions were next placed on three equally spaced points at the centre of the strip. After waiting 3 hours to allow the system to come to equilibrium, a potential of 175 volts supplying 0·12 mA per cm. width of paper was applied.

The chromatograms showed a greater mobility for normal adult than for fœtal hæmoglobin, while test samples from the affected members of the family behaved like the normal adult pigment. This was expected, because in this condition the ratio of hæmoglobin F to adult hæmoglobin is about 1 to 8.

The separation of mixtures of adult and fœtal hæmoglobins by electrophoresis is difficult. Waris (1954) was unable to separate these two hæmoglobins by this method, and found that the mixture behaved as adult hæmoglobin.

*Solubility*

The solubility of the reduced forms of the hæmoglobins in strong phosphate buffer solutions was determined by the method of Itano (1953). In a series of normal adults we found the solubility of reduced hæmoglobin in 2·58*M* phosphate buffer at 25°C to range from 1·28 to 1·52 g. per litre, with a mean value of 1·43 g. per litre, and using cord blood, the range of solubility was 2·34 to 2·93 g. per litre with a mean value of 2·59 g. per litre. Itano found the solubility of adult hæmoglobin under similar conditions to be 1·39 ± 0·15 g. per litre. The table shows that whereas the result of hæmoglobin solubility for the mother is within the normal adult range, those for her children were both raised. Itano's values in thalassæmia minor and major are 1·54 g. per litre and 2·30 g. per litre respectively.

## Discussion

The clinical manifestations of thalassæmia in this family included anæmia, mongoloid facies, epicanthic folds, jaundice, and enlargement of the spleen. The red cells showed poikilocytosis, polychromasia, microcytosis, macrocytosis, target-cells, and basophilic stippling. Nucleated red cells were found in the blood of the three affected members of the family, and the osmotic fragility of the red cells was reduced both before and after incubation. The mean corpuscular-volume was either within the normal range or increased, but Matoth et al. (1955) found a high M.C.V. in thalassæmia amongst Kurdistan Jews and suggested that the large flat cell might be characteristic of this racial group. An analogous situation may exist in this family. In the son there was a striking increase in the number of circulating normoblasts after splenectomy, as has been repeatedly observed in thalassæmia.

Alkali-resistant hæmoglobin, presumably identical with hæmoglobin F, was demonstrated in the blood of

HÆMATOLOGICAL INVESTIGATIONS

| — | Affected members | | | | | Normal members | | |
|---|---|---|---|---|---|---|---|---|
| | Mrs. A | Son | | Daughter | Grandson | Mr. A | Mr. A's sister | Mrs. A's half-sister |
| | | Before splenectomy | After splenectomy | | | | | |
| R.B.C. (millions per c.mm.) | 3·85 | 2·8 | 3·23 | 3·9 | .. | 5·48 | 4·1 | 5·03 |
| Hb (g. per 100 ml.) | 9·5 | 7·0 | 7·9 | 10·1 | 12·5 | 15·8 | 12·8 | 13·5 |
| Hæmatocrit (%) | 34 | 24 | 30 | 35 | .. | 49 | .. | 45 |
| M.C.V. (c.µ.) | 88 | 85 | 93 | 89 | .. | 89 | .. | 90 |
| M.C.H. (µµg.) | 24 | 25 | 21 | 26 | .. | 28 | 31 | 27 |
| M.C.H.C. (%) | 28 | 29 | 26 | 28 | .. | 32 | .. | 30 |
| Reticulocytes (%) | 5·2 | .. | 10·2 | 2·6 | 6·0 | 0·1 | .. | 0·8 |
| Normoblasts (per 100 W.B.C.) | 2 | 19 | 269 | 14 | 0 | 0 | 0 | 0 |
| W.B.C. (thousands per c.mm.) | 5·2 | 5·8 | 12 | 8·2 | 19·3 | 8·4 | 5·5 | 9·1 |
| Platelets (thousands per c.mm.) | 448 | 523 | 1884 | 308 | .. | 538 | 320 | 550 |
| Icterus index | 15 | 20 | 20 | 30 | .. | 5 | 5 | 5 |
| Osmotic fragility (% saline): | | | | | | | | |
| Not incubated | 0·39–0·20 | .. | 0·36–0·20 | 0·45–0·20 | .. | 0·45–0·33 | .. | .. |
| Incubated | 0·39–0·20 | .. | 0·48–0·20 | .. | .. | 0·57–0·33 | 0·63–0·42 | .. |
| Macrocytes | ++ | .. | +++ | ++ | + | – | – | – |
| Microcytes | +++ | .. | +++ | +++ | ++ | – | – | – |
| Hypochromia | ++ | .. | ++ | ++ | + | – | – | – |
| Target-cells | + | .. | ++++ | + | ++ | – | – | – |
| Basophilic stippling | + | .. | + | + | + | – | – | – |
| Hæmoglobin F (%) | 12 | .. | 11 | 18 | .. | 1·8 | 0·8 | 1·6 |
| Hb solubility (g. per litre) | 1·42 | .. | 1·75 | 1·74 | .. | 1·49 | .. | .. |

patients with thalassæmia by Singer et al. (1951). Its presence is not specific for this disease as it has also been reported in sickle-cell anæmia and (in very low concentrations) in hereditary spherocytosis, aplastic anæmia, pernicious anæmia, leukæmia, and myelophthisic anæmia. It has also been described in less well-defined hæmolytic states (Lorber 1955). The concentration of hæmoglobin F varies with the type and severity of the thalassæmia, values ranging from 40 to 100% being reported in thalassæmia major and lesser amounts in thalassæmia minor (Terry et al. 1954). Electrophoretic mobility, solubility, and sickle-cell preparation tests, were done to exclude other abnormal hæmoglobin constituents.

It is generally believed that the disease is inherited as a simple dominant and that the severe form, or thalassæmia major, is homozygous, while the milder form, thalassæmia minor, is heterozygous. This classification is arbitrary, for transitional forms of the disease are found in both groups, ranging from morphological changes in the red cells only to the most severe hæmolytic syndrome, resulting in death within the first few years of life. All the affected members of this family fit best, from their clinical and hæmatological findings, into the thalassæmia minor group. The pattern of inheritance in this family is through the mother to her son and daughter and her grandson, all four being presumably heterozygous in respect to the thalassæmia gene. Although there is no known mixture with Mediterranean stock, a long-forgotten Mediterranean ancestor cannot be excluded. This is suggested by the occurrence of the Rh chromosome cDe or Ro, which is relatively rare in most Europeans, somewhat more common in Mediterranean areas, and frequent in many African populations.

This hæmolytic syndrome is most often called Mediterranean anæmia. Though most reported patients were of Mediterranean ancestry, enough have been reported in other peoples to make this name inappropriate. As long as it is considered a disease existing only in people of Mediterranean extraction, the possibility of it occurring in other racial groups will be overlooked. It must be considered in the differential diagnosis of any hereditary hæmolytic anæmia. Thalassæmia, though referring to the sea, puts no specific geographical boundaries on the disease (Dameshek 1955), and would seem to be the best term to use for the present.


### Summary

A Scottish family, with no known Mediterranean ancestors, contained four members with clinical, hæmatological, and biochemical manifestations of thalassæmia.


We are indebted to Dr. Bruce Chown for the blood-grouping and his many valuable suggestions, to Dr. F. D. White for his interest and coöperation, to Dr. G. C. Stevens for permission to study his patients, and to Mrs. Lillian McLennan and Miss Audrey Kerr for technical assistance.

#### REFERENCES


Bywaters, E. G. L. (1938) *Arch. Dis. Childh.* **13**, 173.
Cooley, T. B., Lee, P. (1925) *Amer. J. Dis. Child.* **30**, 447.
— — (1932) *Ibid*, **43**, 705.
— Witwer, E. R., Lee, P. (1927) *Ibid*, **34**, 347.
Dameshek, W. (1955) *Blood*, **10**, 293.
Dhayagude, R. G. (1944) *Amer. J. Dis. Child.* **67**, 290.
Diwani, M. (1944) *Arch. Dis. Childh.* **19**, 163.
Freudenberg, E., Esser, M. (1942) *Ann. pœdiat.* **158**, 128.
Grinnan, A. G. (1935) *Amer. J. Roentgenol.* **34**, 297.
Itano, H. A. (1953) *Arch. Biochem.* **47**, 413.
Lorber, M. (1955) *J. Mt Sinai Hosp.* **21**, 247.
Matoth, Y., Shamir, Z., Freundlich, E. (1955) *Blood*, **10**, 176.
Minnich, V., Na-Nakorn, S., Chongchareonsuk, S., Kochaseni, S. (1954) *Ibid*, **9**, 1.
Prouty, M. (1950) *Amer. J. Dis. Child.* **79**, 99.
Saracoglu, K. (1943) *Wien. med. Wschr.* **93**, 217.
Schieber, C. L. (1945) *Lancet*, ii, 851.
Schwartz, S. O., Mason, J. (1949) *Blood*, **4**, 706.
Silver, H. K. (1950) *Amer. J. Dis. Child.* **80**, 767.
Singer, K., Chernoff, A. I., Singer, L. (1951) *Blood*, **6**, 413.
Terry, D. W., Motulsky, A. G., Rath, C. E. (1954) *New Engl. J. Med.* **251**, 365.
Waris, E. (1954) *Acta med. scand.* **148**, 167.
Whipple, G. H., Bradford, W. L. (1932) *Amer. J. Dis. Child.* **44**, 336
White, F. D., Delory, G. E., Israels, L. G. (1950) *Canad. J. Res.* **28**, 238.


## URETERIC CATHETERISATION


G. C. TRESIDDER
M.B., B.S. Lond., F.R.C.S.
ASSISTANT SURGEON, THE LONDON HOSPITAL


PLASTIC and nylon ureteric catheters which are now available have the advantage over the gum-elastic type that they can be sterilised by boiling. Catheterising cystoscopes that are boilable can also be obtained. By the following procedures ureteric catheters can be passed aseptically.

### Method

Ureteric catheters should be stored by being laid out straight on the tray of a formalin cabinet. From this a catheter is taken out and passed through a piece of $^1/_2$-in. Penrose tube (made of soft latex rubber). The tube should be a little longer than the catheter and open at both ends. The catheter, covered by the tube, is boiled for five minutes. The two are then taken from the steriliser and placed on the sterile table. The Penrose tube, with the catheter inside, is placed over the rubber nipple of the cystoscope and the catheter threaded through it for a few centimetres. The end of the Penrose tube is then drawn over the rubber nipple.

The patient, with the knees supported, lies on an X-ray table, or better still on a cystoscopic X-ray table. The legs are covered with sterile leggings, and a sterile towel is spread over the lower abdomen. The external urinary meatus is cleaned with boric acid lotion (isotonic solution consisting of gr. 8 to the fluid ounce). In the case of men a dry swab is left on the scrotum under the penis; in women a dry swab is left between the labia.

The cystoscope is passed and the bladder examined. If the cystoscope is of the Brown-Buerger type the examining telescope is withdrawn and the bladder emptied. A sterile towel is then placed under the buttocks. The catheterising part—trailing the ureteric catheter covered by the rubber tube—is inserted into the sheath of the cystoscope and the bladder re-filled with water.

The ureteric catheter can be easily gripped and manipulated through the rubber. After passing some centimetres of catheter it is necessary to pull back the rubber tube, which gets rucked up near the nipple. In this way the ureteric catheter can be passed without the operator touching it and without it touching anything. The rubber tube is taken off when the tip of the catheter is correctly sited—for a pyelogram just inside the pelvis of the ureter, or for a ureterogram just engaged in the ureteric orifice (Tresidder 1954). A renal specimen of urine can be collected and then the radio-opaque solution injected for the radiographic examination.

If the collection of renal urines is incidental to the investigation and unlikely to be of diagnostic importance, a short course of sulphonamide tablets and citrate mixture may be begun the day before the instrumental investigation. If urinalysis, culture, and animal inoculation are included in the investigation, the course should be begun immediately after instrumentation.

Even if this procedure is not adopted routinely for all ureteric catheterisations, I strongly recommend its use in the investigation of hydronephrotic and non-functioning kidneys. In these cases of obstruction, unless such special precautions are taken, the renal pool of residual urine is likely to become infected as a result of ureteric catheterisation (Tresidder 1954).

By this aseptic method of ureteric catheterisation together with the sulphonamide and citrate therapy, it may be possible to lessen the incidence and severity of subsequent reactions and infections.

#### ADDENDUM

I have lately used the same method for sterilising and passing urethral catheters of rubber or plastic.

The urethral catheter is inserted into half a length of 1-in. Penrose tube. The two are placed in the steriliser and boiled for five minutes, after making sure that there is water, but no air, inside the catheter and between it and the Penrose tubing.

Next the hands are washed, the external urinary meatus is cleaned with boric acid lotion, and a sterile towel is placed over and between the thighs. In men, jelly lubricant or anæsthetic is squeezed out from its tube into the urethra. The catheter, inside the Penrose tube, is then picked up and passed into the urethra.

The Penrose tube is thin enough to allow the fingers to get the feel of the catheter, and no difficulty has been encountered as a result of having the catheter covered.

I thank Miss P. Bretten, S.R.N., for her help and advice.

REFERENCE

Tresidder, G. C. (1954) *Brit. J. Urol.* **26**, 240.

## RUPTURED UMBILICAL HERNIA

H. DE GLANVILLE
M.A., M.B. Camb.
TEMPORARY MEDICAL OFFICER, COLONIAL MEDICAL SERVICE, GOLD COAST

RUPTURE is an extremely rare complication of umbilical hernia, a relatively common tropical condition. The case reported here is unusual in the apparent absence of any precipitating cause.

### Case-report

An African woman of the Ewe tribe, aged 30, and 7 months pregnant with her fifth child, attended hospital in British Togoland complaining that some tissue had been protruding from her umbilicus for the past 12 hours. She had first noticed the protrusion after feeling some irritation in the region of the umbilicus. There was no pain, and to her knowledge she had had no previous lesion such as a boil or ulceration at that site. She denied any coughing or straining, and said she was not aware of ever having had an umbilical hernia.

A narrow tail of omentum, 2 in. long, projected from a small orifice about $^1/_8$ in. in diameter at the edge of the umbilicus. She was otherwise healthy and about 30 weeks pregnant. Temperature 99°F; pulse 92 per min.

The soiled omental tag was excised and a Mayo repair carried out under general anæsthesia. Her progress was uneventful, and, ignoring advice to be confined under supervision, she delivered normally at home 2 months later.

### Discussion

Five cases of ruptured umbilical hernia have been recorded. McGrath (1918) reported the case of an old lady of 78 who, while straining at stool, ruptured a hernia which she had had for 40 years, and which had recently enlarged. Hunziker (1946) noted a similar case in which the rupture occurred during an epileptic fit. MacLean (1950) described an infant aged 3 months in whom rupture followed a severe bout of crying, and Ninh and Hoanh (1951) reported a similar case in a malnourished infant of 20 days, whose cord had separated on the 12th day after birth. Lastly, Rupnik and Brown (1953) described the rupture of a long-standing umbilical hernia in a man of 56 with cirrhosis of the liver and ascites, admitted to hospital for the treatment of diarrhœa.

The patient removed his abdominal binder and rose from bed, with consequent rupture of the hernia, the escape of much ascitic fluid, and the protrusion of an omental tag. The broken skin showed signs of gangrene. Rupnik and Brown suggested the rupture may have been due to pressure necrosis from the binder, local venous engorgement (caput Medusæ), or raised intra-abdominal pressure due to the ascites and the rise from bed.

Umbilical herniæ are common in West African children, but spontaneous improvement or cure often occurs. Careful examination of the umbilical scar, however, sometimes shows a residual weakness or bulging of which the patient may be unaware; such a defect was probably present in my patient. Treatment is seldom undertaken because complications such as strangulation are rare, and the mothers will not strap their children's abdomens for the prolonged period necessary. I have, however, seen extensive ulceration of the thin skin overlying a large umbilical hernia which ruptured, with fatal results, in an elderly African woman.

In the case described there was probably an unrecognised hernial defect, but the absence of any precipitating strain, which may be blamed for the ruptures in the other cases cited, is an unusual feature.

I am indebted to Dr. E. Akwei, chief medical officer of the Ministry of Health, Gold Coast, for permission to publish this paper, and to Dr. P. H. Canham of the Medical Field Units, for assistance at the operation.

REFERENCES

Hunziker, W. (1946) *Schweiz. med. Wschr.* **76**, 991.
McGrath, W. J. (1918) *J. Amer. med. Ass.* **71**, 1650.
MacLean, A. B. (1950) *Brit. J. Surg.* **38**, 239.
Rupnik, E. J., Brown, R. P. (1953) *U.S. Forces med. J.* **4**, 747.
Tran Ngoc Ninh, Dao Duc Hoanh (1951) *Extreme-orient Med.* **4**, pt. 2, 52.

## CEREBRAL CŒNURIASIS IN MAN

KENNETH C. WATSON
M.D. Aberd.
ASSISTANT PATHOLOGIST, NATAL PROVINCIAL ADMINISTRATION
WILLIAM LAURIE
D.S.O., M.D. Glasg.
SENIOR PATHOLOGIST, NATAL PROVINCIAL ADMINISTRATION
*From the Department of Pathology, Edendale Hospital, Pietermaritzburg, South Africa*

CEREBRAL cœnuriasis is caused by infestation of the brain by larvæ (*Cœnurus cerebralis*) of the tapeworm *Multiceps multiceps*. The adult worm is 40–60 cm. long, and it has a scolex with an armed rostellum. The gravid uterus contains 18–26 branched lateral arms on each side of the main stem. The usual definitive host is the dog, but wolves are also affected. The intermediate hosts are sheep, goats, and cattle, and the central nervous system is usually involved.

Only a very few cases of the larvæ affecting man have been recorded:

The first appears to be that of a Parisian who died in 1911 (Craig and Faust 1943). Necropsy showed the cœnurus, or bladder-worm, in the brain.

Cluver (1940) recorded the disease in a Bantu, the diagnosis being confirmed at necropsy. Clapham (1941) found the condition in a British sailor who died in coma. Buckley (1947) recorded the disease in a girl with paraplegia, and Johnstone and Jones (1950) cited a further example with involvement of the pons, medulla, and interpeduncular space in a child aged 2.

Becker and Jacobson (1951a) described 3 cases, and later (Becker and Jacobson 1951b) a 4th case. All 4 patients came into contact with sheep in their work. The diagnosis in each case was made at operation, and all 4 patients recovered.

We report here 2 cases of cerebral cœnuriasis in man.

### Case-reports

**Case 1.**—A Bantu woman, aged 32, was admitted to Edendale Hospital on Feb. 22, 1955, with a three-month history of headache. The headache was generalised but occasionally it was more pronounced in the frontal region. For three weeks before admission she had had intermittent attacks of stiffness of the neck muscles, with pain in both legs and general malaise and weakness. The headache was getting worse. There was no history of any visual upset.

*On examination* she looked ill; her temperature was 99°F, and her pulse-rate was 74 per min. There was some neck retraction, but Kernig's and Brudzinski's signs were negative. There were no localising signs of a lesion in any part of the central nervous system. The reflexes were normal and there were no motor or sensory changes. The retinæ and optic discs were normal and there were no visual-field defects.

*Investigations.*—Lumbar puncture on the day of admission yielded clear cerebrospinal fluid (C.S.F.) under normal pressure. The protein content was 20 mg. per 100 ml., and the sugar and chloride levels were normal; the cell-count was less than 1 per c.mm. The blood and C.S.F. Wassermann tests were negative. Blood-urea level was 30 mg. per 100 ml. Hæmoglobin level and total white-cell count were within normal limits. Radiographs of the skull and chest were normal.

*Progress.*—The patient remained in hospital for four weeks, and during this time she improved considerably, with some relief of her headache and neck stiffness. But on March 26 she suddenly collapsed and died.

*Necropsy.*—The cerebral convolutions were considerably flattened, and the sulci obliterated. There was pronounced upward bulging of the tentorium cerebelli, and severe internal hydrocephalus with a large rupture of the floor of the third ventricle. The right cerebellar hemisphere was greatly enlarged by a cystic tumour which invaded the cerebellar tissue and projected from the surface of the cerebellum. The surface of this tumour consisted of grape-like processes. Histological examination of the cerebellum showed numerous cysts typical of those found in infestation with *Cœnurus cerebralis*. Many of the cysts were sterile (this seems to be characteristic of the condition).

**Case 2.**—A Bantu man, aged 33, was admitted to hospital and died in coma. No history was available.

*Necropsy* showed a cystic mass, destroying the left occipital lobe and projecting from the surface of the brain. The mass was about 1 in. in circumference. A similar, but smaller, cystic lesion was present in the right occipital lobe, and a third collection of small grape-like cysts was present in the right temporal lobe. The cysts contained a scolex and hooklets typical of *Multiceps multiceps*. There were no lesions below the tentorium cerebelli.

### Discussion

These cases of cerebral cœnuriasis are recorded because the condition may be commoner than is realised, especially in sheep-raising areas where there are many dogs. Operation is often successful in this disease, and all 4 cases reported by Becker and Jacobson (1951a and b) recovered after operation.

In most of the previously reported cases there have been changes in the C.S.F., with a rise in the pressure and protein level, and lymphocytosis. In our first patient the C.S.F. was normal on admission and also four days later. In view of the necropsy findings, it is probable that the absence of abnormalities in the C.S.F. was due to complete obstruction of the foramina of the fourth ventricle.

The relation of the lesions to the C.S.F. pathways and the localisation in the posterior fossa appear to be characteristic of cerebral cœnuriasis. Becker and Jacobson (1951a) said that *Cœnurus cerebralis* is usually responsible for parasitic infestation, especially of the racemose type, of the posterior fossa. They found papillœdema in all of their 4 cases, but it was absent from our first patient. This sign, reflecting increased intracranial pressure, may appear late.

Cerebral cœnuriasis can be diagnosed during life only at operation, because the clinical picture is one of increased intracranial tension only. Becker and Jacobson (1951a) found the hydatid complement-fixation test positive in 2 cases, presumably because the two parasites share a common antigen. This test, therefore, will not distinguish cœnuriasis from cysticercosis.

We thank Dr. R. E. Stevenson, director of the provincial medical and health services, Natal, for permission to publish this paper, Dr. J. D. Woods for access to the clinical notes, and Dr. G. Roach for the histological report.

### REFERENCES

Becker, B. J. P., Jacobson, S. (1951a) *Lancet*, ii, 198.
— — (1951b) *Ibid*, p. 1202.
Buckley, J. J. C. (1947) *Trans. R. Soc. trop. Med. Hyg.* **41**, 7.
Clapham, P. A. (1941) *J. Helminth.* **19**, 84.
Cluver, E. H. (1940) *Rep. S. Afr. Inst. med. Res.* p. 49.
Craig, C. F., Faust, E. C. (1943) Clinical Parasitology. London, 3rd ed.; p. 452.
Johnstone, H. G., Jones, O. W. jun. (1950) *Amer. J. trop. Med.* **30**, 431.

# Medical Societies

## AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

THE association met at the University of Illinois, Chicago, on Nov. 3.

At the clinicopathological conference in the morning Dr. SHEILA SHERLOCK (London), the guest speaker, emphasised the importance of careful attention to clinical assessment. Dr. HANS POPPER (Chicago) demonstrated the pathological sequence of portal cirrhosis, cholelithiasis, and pancreatitis which was responsible for complex clinical findings.

Prof. R. M. KARK (Chicago), the chairman, introduced the speakers for the afternoon and evening sessions.

### Glucose Metabolism

The central position of the liver in carbohydrate metabolism and the importance of the hexose-monophosphate shunt were discussed by Dr. P. K. BONDY (Yale). Although inadequate maintenance of blood-glucose, slow clearing of exogenous glucose, and reduced availability of metabolites might be anticipated in liver disease, a glucose-tolerance curve of a mild diabetic type and possibly poor tissue repair due to ribose deficiency were the only objective findings, while hypoglycæmia was surprisingly rare.

### Protein Metabolism

Dr. C. S. DAVIDSON (Harvard) suggested that dietary deficiency was the most important factor in the protein malnutrition of alcoholic liver-disease. Pancreatic disease might be a contributory factor, but amino-aciduria was rarely of significance. Recovery was slow owing to the liver disease, and improvement in hepatic function during treatment was reflected by increased albumin synthesis.

### Ammonia and Coma

Dr. L. T. WEBSTER (Harvard and Cleveland) had shown that acetazolamide ('Diamox') caused an "endogenous" rise in blood-ammonia levels, and that ammonia was liberated from the brain under such circumstances. In contrast, a relative uptake of ammonia occurred in the brain when oral protein, intravenous urea or ammonium chloride were given to one patient. During impending hepatic coma and coma, patients with an exogenous source of nitrogen (dietary protein, gastro-intestinal bleeding, or elevated blood non-protein nitrogen) showed an uptake of ammonia in the brain, whereas those in "endogenous" coma did not. By sampling from abdominal-wall vessels, Dr. Webster had found a rapid rise in portal-vein ammonia levels within two hours of a protein meal. Further investigation suggested that the source of this ammonia was glutamine.

From London Dr. SHERLOCK (S. Sherlock, E. A. Phear, B. Ruebner, and W. H. J. Summerskill) reported that oral *dl*-methionine might precipitate impending hepatic coma in patients with liver disease without alteration in blood-ammonia levels, and that this effect could be prevented by the simultaneous administration of aureomycin.

Dr. W. W. FALOON, together with Dr. J. AUCHINCLOSS, Dr. E. HOWLAND, and Dr. R. GILBERT (New York), concluded from venous-catheterisation studies that peripheral-blood ammonia was largely derived from portal blood following portacaval anastomosis. They considered that considerable uptake of ammonia by the tissues occurred in the cirrhotic patient, and postulated that the lungs might be a source of ammonia since arterial levels were higher than those in the right auricle.

The co-enzyme factor, thioctic (lipoic) acid, had been exhibited in hepatic coma by Dr. P. LISAN, together with Dr. J. M. GAMBESCIA, Dr. C. M. THOMPSON, and Dr. M. FUCHS (Philadelphia) with apparently favourable effect in three of five patients. Blood-levels of pyruvate and lactate fell on administration of the drug.

Dr. SUMMERSKILL (London and Harvard) with Dr. SHERLOCK and Dr. E. A. DAVIDSON showed that the

syndrome of hepatic coma was occasionally a chronic neuropsychiatric disorder in patients with cirrhosis and an extensive portal collateral circulation and that restriction of dietary protein resulted in dramatic improvement.

In the discussion Dr. SHERLOCK emphasised her opinion that elevated blood-ammonia levels after portacaval anastomosis were due to the coincident liver disease together with the deviation of portal blood.

Dr. W. VOLWILER (Seattle) commented that a group in Denver had succeeded in reproducing the characteristic features of impending hepatic coma by the intravenous infusion of large amounts of ammonium chloride in subjects without liver disease.

Dr. P. YOUNG (Cincinnati) had found that blood introduced into the stomach, thus reproducing the effect of gastrointestinal bleeding, produced abnormal blood-ammonia curves in patients with liver disease.

### Some other Communications

Dr. I. B. BRICK and Dr. L. KYLE (Washington) had investigated the effect of methyltestosterone in patients with liver disease. Despite the recognised hazard of testosterone jaundice, there was no change in liver-function tests or hepatic histology in their patients.

The application of needle biopsy to the diagnosis of primary or secondary malignant hepatic lesions was described by Dr. M. STAUFFER (Mayo Clinic), who had found that 83% of neoplasms were revealed by this method. These results, however, were achieved by taking multiple biopsies, often from a prominent tumour and with the help of frozen sections.

The possibility that the recently described syndrome of chronic idiopathic jaundice with unidentified pigment in the liver cells might be relatively common was raised by Dr. M. CAMPBELL (Minnesota). Together with Dr. J. COE and Dr. F. W. HOFFBAUER he reported three instances of this condition; all were in elderly men, one of whom had retinitis pigmentosa.

Another congenital disorder of uncertain ætiology had been studied by Dr. I. M. ROSENTHAL and Dr. H. J. ZIMMERMAN (Chicago) who described the onset of jaundice with tremor, ataxia, and scanning speech during childhood. As in cases reported earlier, liver biopsy was normal, and it was concluded that this non-hæmolytic, non-obstructive icterus was due to an inability of the liver cells to excrete bilirubin.

Dr. A. L. SCHERBEL (Cleveland), described a patient with normocholesteræmic xanthomatosis, hepatic fibrosis, and pulmonary cholesterolosis. Xanthomatous deposits had caused conjunctivitis and polyarthritis.

Dr. I. A. SCHAFER (Atlanta) and his colleagues (H. F. Eichenwald, J. Mosely, J. I. Karush, T. A. Asher, M. L. Candler, and G. R. Cooper) reported findings from an epidemic of infectious hepatitis in Kentucky. There was a high incidence of myalgia (56% of patients) and backache (36%) in the acute episode, and the persistence of symptoms or signs (52%) or abnormal laboratory findings (35%) a year after apparent recovery was of interest.

Radioactive rose-bengal using $^{131}I$ had been applied to a study of liver function by Dr. C. H. BROWN (Cleveland). The uptake was recorded by a scintillator over the liver. In hepatic disease the uptake was reduced and excretion was delayed, but similar findings in obstructive jaundice reduced the diagnostic value of the test.

Dr. D. MOLANDER and Dr. M. A. PAYNE (New York) found elevated levels of S.G.O. transaminase in patients with decompensated cirrhosis, and abnormally high values also occurred in hepatitis and biliary cirrhosis.

Dr. A. G. BEARN (New York) discussed the place of dimercaprol (BAL) in the treatment of Wilson's disease. Some patients showed a good response, and when the result was less satisfactory he advocated a trial of larger doses continued over a long period.

Dr. F. L. IBER, Dr. L. L. UZMAN, Dr. M. KNOWLTON, and Dr. T. C. CHALMERS (Washington) considered that the affinity of the liver for copper in Wilson's disease was due to an electrophoretically distinct factor which they had demonstrated. They were unable, however, to identify this factor with cœruloplasmin.

## Reviews of Books

### Subphrenic Abscess

H. R. S. HARLEY, F.R.C.S., consultant thoracic surgeon to the United Cardiff Hospitals. Oxford: Blackwell Scientific Publications. 1955. Pp. 216. 35*s*.

BASED on 188 cases of subphrenic abscess from hospitals in or near London, this book examines the condition from all angles.

The anatomy of the subphrenic region is discussed, and five intraperitoneal and two extraperitoneal spaces are described. This involves a clarification of the arrangement of the ligaments attached to the liver and their behaviour if the liver is separated from its normal relations by air or fluid. Most subphrenic abscesses occur on the right, and nearly all are intraperitoneal involving one space.

90% of the abscesses were secondary; perforated peptic ulcers, appendicitis, or abdominal operations were associated with two-thirds. The bacteriological investigations gave equal proportions of pure and mixed infection, and less than 10% were sterile. *Staphylococcus aureus* and streptococci were responsible for "pure" infections, and in "mixed" infections, *Escherichia coli* was invariably present as well. Mr. Harley holds that infection spreads by a direct intraperitoneal route and not by lymphatics, and he discusses the various changes in intraperitoneal pressures that occur in different postures and during respiration. Pleural effusion was recorded in 25% of the 188 cases, and is regarded as analogous to œdema found in relation to an inflammatory focus.

Among the clinical features high fever, tachycardia, leucocytosis, and anæmia were common, but where the abscess was chronic one or more of these signs was absent. The radiological signs included immobility of the diaphragm often associated with elevation, and sometimes with gas below it.

Drainage of the abscess should always be undertaken so as to avoid the pleural cavity and prevent collapse of the lung and total pleural infection. The incision differs according to the location of the abscess and the space involved, and once drainage has been established the control of healing should be observed by injection of lipiodol and radiography, so that the tube is not removed prematurely.

The over-all mortality in the 188 cases was 40%—an alarmingly high figure. Earlier diagnosis, followed by chemotherapy and adequate drainage, now offers better prospects.

Mr. Harley has written a classic on the subject. The case analysis is detailed, the bibliography carefully considered, and the opinions soundly based. It will be surprising if many of his views do not find a permanent place in the textbooks of the future.

### Asclepiades, his Life and Writings

Translated by the late ROBERT MONTRAVILLE GREEN, M.D., emeritus professor of anatomy, Harvard Medical School. New Haven, Connecticut: Elizabeth Licht. 1955. Pp. 167. $6.

Asclepiades, who practised medicine in Rome in the golden age of Cicero, Horace, and Virgil, was the most important physician between Hippocrates and Galen, yet singularly little is known about him. Unhappily almost all his works have perished except for a few fragments from which Dr. Antonio Cocchi wrote a biography that was indifferently translated into English in 1762. The first part of this book consists of a new translation of this work. Thirty years later Christian Gottlieb Gumpert collected fragments of the writings of Asclepiades and published them with his comments in Weimar. Only one copy is extant and from it the present translation has been made.

Many innovations have been attributed to Asclepiades. He was the first to associate hydrophobia with the bite of rabid animals. He advocated walking in sand for paralysis, gave specific prescriptions of music for the mentally ill, and used massage for muscle spasm as well as dry steam and radiant heat.

The translator, "a gentle scholar," did his work well. Here is an excerpt:

"The chief value of music, according to the opinion of Asclepiades, is to be found in those diseases in which the mind

is affected. Hence the minds of phrenitics, disturbed by disease, are often restored to their own nature by a symphony. In the same way he teaches that a song should be employed in the treatment of mania. Cælius speaks thus 'they use also madrigals of pipes with varied modulations: one of these is gay and excites those known to be insane from sorrow; another is serious, injecting sternness, as in war, in those who are affected with laughter or girlish giggling.'"

### Clinical Papers and Essays on Psychoanalysis

KARL ABRAHAM, M.D. Translators: Hilda C. Abraham, M.D., D. R. Ellison, M.A. London: Hogarth Press and Institute of Psychoanalysis. 1955. Pp. 336. 25*s*.

IN 1927 when Karl Abraham's Selected Papers were published as a volume in the International Psycho-analytical Library, Dr. Ernest Jones said that the book contained the whole of Abraham's more important psycho-analytical work, except Traum und Mythus, and the study of Amenhotep IV. In the ensuing quarter of a century Abraham's reputation has increased, his pupils have in their turn become prominent psycho-analytical teachers and theorists (though in the process they have diverged widely from one another), and it has been for some time obvious that psycho-analysts unable to read German needed a satisfactory translation of those papers.

Though less influential and important than those selected in 1927, the papers nevertheless contain clinical observations, applications of psycho-analysis to biography and mythology, and some polemical or expository writings which are all of value to students of this subject. It is fortunate that his daughter, herself a psychiatrist well versed in psycho-analysis, has been able to translate and edit these essays and articles. Among the more elaborate studies are the anthropologically ingenuous but psycho-analytically original and inventive monograph on Dreams and Myths (previously translated in the Nervous and Mental Disease Monograph Series), and Abraham's sympathetic and penetrating effort to understand the psychology of the painter Giovanni Segantini.

Abraham's intellectual integrity and singlemindedness are plain in these as well as in the other writings presented in this volume. The translation is clear and straightforward, though a few German idioms have been retained.

### Über den Einfluss der Schwangerschaft auf die Lungentuberkulose

Dr. med. KLAUS OBMANN, Erfurt. Leipzig: Georg Thieme. 1955. Pp. 142. DM.25.

THE influence of pregnancy on tuberculosis is a subject of lasting interest. This well-produced book records experience at the clinic for the town and county of Jena in Eastern Germany.

The greater part is occupied by the case-histories of 347 women with pulmonary tuberculosis during 531 pregnancies between 1930 and 1952. Many of the histories are illustrated by the graphic method of Brauening and by radiographs. Relapse in the tuberculosis was commonest in the postpartum period, though it was by no means uncommon in the first months of pregnancy. Patients who aborted spontaneously or whose pregnancies were terminated did better. On the other hand, suckling was thought to be beneficial.

As for treatment, collapse therapy receives more emphasis than chemotherapy. The author feels that termination of pregnancy is not really treatment, and he favours strictly limited indications for interference, though he is not against it altogether.

Despite its satisfactory presentation of a great deal of material, the book seems outdated because it does not take fully into account the great changes that chemotherapy has produced.

### Classics of Biology

AUGUST PI SUÑER. London: Pitman. 1955. Pp. 337. 35*s*.

IT was an excellent idea to sketch the evolution of several broad facets of biology and to illustrate them with important milestones (reprints of original articles from Aristotle to the present day).

The subjects discussed are: matter and energy in life; cell theory; stimulus and excitation; biocatalysts; metabolism; growth and reproduction; germ-cells and soma; form and dynamics of reproduction; heredity; individual and species; preformation and epigenesis; life on earth; geography and palæontology; causation and design; reflexes, consciousness, and will; and, finally, the whole and its parts (holism, &c.).

The reader obtains a bird's-eye view of an extensive field of evolution together with a running commentary on the philosophic implications.

### Cardiac Auscultation

*Including Audio-visual Principles.* J. SCOTT BUTTERWORTH, M.D., associate professor of medicine, New York University Post-Graduate Medical School; MAURICE R. CHASSIN, M.D., assistant professor of clinical medicine; ROBERT MCGRATH, M.D., associate professor of clinical medicine at the school. New York and London: Grune & Stratton. 1955. Pp. 105. $4.50.

WELL illustrated, written, and produced, this book describes and demonstrates with clarity the findings of auscultation. The phonocardiograms are perfectly satisfactory. This should be a very valuable method of teaching and is of course already used, in a less complete way, by many clinicians; but, though in principle the book is excellent, it cannot escape some criticisms.

The outlook is rather too anatomical and would surely be much improved for teaching purposes if there were more hæmodynamic principles. For example, it would be helpful to explain the gap between the second heart-sound and the onset of a mitral diastolic murmur. The current view that auricular and third heart-sounds are "filling sounds" is not mentioned, and gallop rhythm is said to occur almost invariably with heart rates of 100 or more, so that by this definition only summation gallop can be considered. Not many clinicians would agree that an early diastolic murmur indicates pulmonary incompetence, rather than aortic incompetence, if there is no waterhammer pulse; and the second sound in atrial septal defect is described as accentuated. European progress in auscultation since Laennec is largely ignored, and the monaural wooden stethoscope is said to be still in common use in Europe.

Each illustration is a single phonocardiogram without time-marker or reference tracing. This aids clarity, but some valuable clinical points are missed. The aortic and pulmonary components of the second sound cannot be identified and there is no description of the wide splitting of the second sound in the pulmonary area which is so useful in the diagnosis of atrial septal defect and bundle-branch block. There is no mention of the retention of a normal aortic component, with a delayed or absent pulmonary component, in pulmonary stenosis.

The clinical side is therefore rather disappointing but the discussion of the principles of hearing and the stethoscope is excellent.

---

**Cardiovascular Surgery** (Philadelphia and London: W. B. Saunders. 1955. Pp. 543. 89*s*.).—The proceedings of the international symposium on this subject held at the Henry Ford Hospital, Detroit, last March, have been published under the editorship of Dr. Conrad R. Lam. Those taking part included Sir Russell Brock, Dr. Ian McMillan, and Prof. C. G. Rob.

**Mechanisms of Microbial Pathogenicity** (Cambridge: University Press for the Society for General Microbiology. Pp. 333. 25*s*.).—On April 19 and 20, 1955, the Society for General Microbiology held its fifth symposium in London, and this is a record of the sixteen contributions. A book of this kind can be neither complete nor homogeneous; for some contributors take the opportunity to develop their own views, while others give a well-balanced review in which their own work can be seen in proper perspective. The solution might be to give a general review of each aspect of the subject under discussion, and then to let the specialists with divergent views have their say. Unfortunately the time limit on most symposia forbids such comprehensive treatment. As this book was published before the symposium was held, the discussion could not be included, and controversial views must go unchallenged. The difficulty, therefore, for the general reader is to know what can be accepted as reasonably established and what is still hotly contested; but the specialist will find much that is stimulating.

THE LANCET
*LONDON: SATURDAY, DEC. 24, 1955*

## Continuous Chemotherapy of Tuberculosis

THERE have been no striking additions to the antituberculous drugs since isoniazid appeared three years ago. But an important change has come about in the way they are used; and surprisingly little has been said about it. The chemotherapy of tuberculosis has evolved in this country largely from the foundations laid by the Medical Research Council's clinical trials, in which the duration of treatment was limited for the purposes of the experiment to periods of a few months only. The facts discovered were very valuable; but more has been inferred from them than is justified, for the investigations were not designed to answer the question how long antibacterial drugs can safely and usefully be given. At first streptomycin was scarce and rationed, and by the time it became freely available and the addition of *p*-aminosalicylic acid (P.A.S.) had reduced the fear of resistance, treatment by conservative bursts of chemotherapy was already well established. In the United States chemotherapy developed under quite different circumstances; and both in clinical trials and everyday practice it appears to have been used in a much more adventurous way. In 1953 we suggested [1] that the risk of bacterial resistance may have been exaggerated and that continued, even life-long, antibacterial treatment might sometimes be justified; and last year we noted [2] that there seemed to be much less opposition to long courses of treatment. On an earlier page of this issue we publish the first full report in this country of the results of such treatment.

Since 1950 Dr. HOYLE and his colleagues have treated 142 patients for nine months or longer, and they have observed 63 of them for more than a year after treatment was stopped. 46 had bilateral disease affecting four or more zones and 92 had cavities in the lungs. All received combinations of two of the three drugs, streptomycin, P.A.S., and isoniazid; and in most of them the streptomycin was given daily for the first three or four months. 119 have been treated for longer than a year and 12 for longer than two years. All but 41 received no other treatment than rest, drugs, and convalescence: of the 41, resection was done in 16 and some form of lung collapse in 25. The results were excellent. Radiographic improvement continued for considerably longer than might have been expected, for half the patients kept on improving after the first six months, which was the longest period of treatment used in the M.R.C. trials. In 64 of the 92 patients with lung cavities, the cavities closed without further treatment. Tubercle bacilli were isolated before treatment in 111; after a year they were found in only 9. Bacilli resistant to streptomycin and P.A.S. were grown at some time from all sputum-positive patients, but only 1 patient in whom resistant strains have been detected has so far deteriorated. 4 patients have died, but death was due to other diseases in 2, and 1 died after a thoracoplasty. 126 patients are leading their normal lives and only 3 are known to be infectious. The most important observations were that no patient has relapsed while under treatment, and that some have relapsed since it was stopped.

STEINIGER and HOWARD, in the United States, report similar striking results with long-continued treatment of patients with less favourable prospects.[3] They treated 300 with rest and chemotherapy for more than a year. Two-thirds had far advanced bilateral disease and slightly less than half were unsuitable for any more radical treatment. By the twelfth month 77% had consistently negative sputum cultures. Only 1 (with long-standing pulmonary fibrosis and emphysema) died while taking the drugs, and 1 died two months after refusing further treatment. DOONEIEF and HITE, of the Montefiore Hospital, New York, who first reported their experience with long-continued chemotherapy in 1954,[4] say in their second report [5] that "tuberculosis of the lung is the . . . most insidious of the relapsing infections:" 15% of those discharged from their hospital in 1951 relapsed in the next three years. Dr. HOYLE and his colleagues mention that 12% of 90 patients discharged from Frimley Sanatorium in 1950 who had received less than seven months' chemotherapy relapsed within three years, although 61 had been treated with collapse or ablation as well. DOONEIEF et al. go further than recommending long periods of treatment: as relapse is so rare while treatment continues, and as it is impossible to predict which patients are going to relapse when it is stopped, they believe that treatment should be continued indefinitely or until some reliable guides to the best length of treatment have been discovered. They have treated 101 patients with pulmonary tuberculosis for periods of twelve to forty-five months, 23 of them for more than three years. 31 had a resection. Only 1 patient (with a manic-depressive psychosis) relapsed under treatment and in that case the lung cavities had not closed. But 2 others relapsed after stopping the drugs against advice. Chemotherapy is continued at home and at work and some patients have even been taught to inject streptomycin themselves. Toxic effects have not been troublesome, and DOONEIEF et al. say that "patient acceptance is good." Nor have Dr. HOYLE and his colleagues found it hard to persuade their patients to take the drugs continuously for long periods. They say that the results make continuous chemotherapy a direct competitor to surgical resection. As we suggested a few months ago,[6] it is a pity that

1. *Lancet*, 1953, ii, 237.
2. *Ibid*, 1954, ii, 691.
3. Steiniger, W. J., Howard, W. L. *Dis. Chest.* 1955, **28**, 177.
4. Dooneief, A. S., Hite, K. E. *Amer. Rev. Tuberc.* 1954, **70**, 219.
5. Dooneief, A. S., Hite, K. E., Bloch, R. G. *Arch. intern. Med.* 1955, **96**, 470.
6. *Lancet*, Aug. 13, 1955, p. 330.

this method of treatment is not being more closely investigated in this country by controlled clinical trials. The rapidly accumulating evidence, mainly unpublished, of the safety and efficacy of long-continued rational chemotherapy with proven combinations of drugs may make such a trial more acceptable. Three years ago, when isoniazid arrived, the idea of using drugs for as long as an artificial pneumothorax would have been much frowned on in this country: "physician acceptance" may now be better.

## Reserpine and the Nervous System

RESERPINE, which first aroused interest as a remedy for hypertension, is now increasingly used in psychiatry. In several disorders, notably schizophrenia, it is widely credited with valued tranquillising effects; but a few controlled studies [1 2] induce a more critical attitude towards its usefulness in psychoneuroses. Research is proceeding along two parallel paths. On the one hand, clinicians are learning to define more precisely the effects of the drug, and to decide what type of patient will respond favourably. At the same time, experimental pharmacologists have been studying its intimate actions on nervous structures, and their findings not only help us to understand its actions but lead to new ideas about organisation within the nervous system.[3]

Many of the effects of reserpine—hypotension, bradycardia, diarrhœa, miosis—suggest an action in the autonomic nervous system, and BEIN [4] first put forward the view that the drug depressed the central control of the sympathetic outflow in the hypothalamus. An extension of this concept by SCHNEIDER [5] indicated that the prime action was not direct sympathetic depression, but rather blockade of those afferent impulses which otherwise provoked efferent sympathetic discharge. The tranquillising effect of reserpine, and the development of parkinsonism after large doses, suggested an additional site of action outside the autonomic nervous system. BEIN failed to demonstrate any effect of reserpine on peripheral nervous structures; but SCHNEIDER gave very large doses of reserpine to cats (doses comparable to those which induce parkinsonism in man) and succeeded in showing that such doses increased the knee-jerk response.[6] This effect was due to facilitation of the passage of impulses across monosynaptic pathways in the spinal cord. Further evidence that reserpine acts in other parts of the nervous system came from the demonstration [7] that it could lower the threshold to convulsive seizures in mice stimulated by electricity. More information about the ability of reserpine to facilitate nervous processes emerged from a study of its characteristic sedative or tranquillising property. Though reserpine usually causes drowsiness, it does not induce narcosis, and persons apparently asleep under its influence can be easily roused. Electroencephalographic records in rabbits,[8] monkeys,[9] and man [10] showed that sleep patterns did not appear in the tracing after full doses of reserpine. This is in sharp contrast to the changes induced by barbiturates. In the normal animal, tactile or auditory stimuli applied during sleep produced characteristic changes in the electro-encephalogram. This "arousal pattern" could also be induced by electrical stimulation of the medullary reticular formation. In the curarised rabbit [8] asleep under the influence of barbiturates, progressively stronger tactile and auditory stimuli and electrical stimulation of the reticular formation were required to produce arousal changes in the electro-encephalogram, and the pattern so induced was itself abnormal. After reserpine in doses up to 1 mg. per kg. the "sleep pattern" was not seen, but the arousal response was produced more easily than in normal sleep, and the threshold of electrical stimulation of the reticular formation was lowered. With larger doses of reserpine the electrographic pattern of alertness was continuously present, replacing the normal rhythm. Thus reserpine facilitated the brain-stem arousal mechanism. Although these findings do not explain why reserpine causes drowsiness, they demonstrate how the sedative effect of reserpine differs from that of barbiturates. It is also known that electrical stimulation of the brain-stem reticular formation in animals can produce a rhythmically alternating tremor which is abolished by atropine.[11] RINALDI and HIMWICH [8] suggest that the capacity of reserpine to stimulate the reticular formation may underlie the parkinsonism produced in man. The facilitation of convulsions [7] is another indication for care in the use of reserpine, and increased frequency of seizures has been noted in epileptics treated with the drug.[12] Reserpine competitively antagonises phenytoin [13] and the two drugs should not be given together. Particular care is also needed when patients under treatment with reserpine are given electroconvulsion therapy.

The physician treating hypertensive patients with relatively small doses of reserpine will be concerned about the mental side-effects of the treatment.[14] The mechanism of this effect can still only be guessed at in terms of facilitation of nervous transmission within the central nervous system. More clinical information is now available.[15–19] Serious mental effects are likely in about 5% of patients under treatment with doses of the order of 1–2 mg. of reserpine daily, or equivalent amounts of whole-root preparations. It seems that treatment must last two months or more before the effects appear. Patients previously in good mental health can be affected but mental changes are commoner in those who were previously unstable.[19] Recovery is the rule but is often slow. The potentialities for good and for ill of rauwolfia alkaloids have not yet been fully explored, and much remains to be learned about what reserpine does in the nervous system.

1. Davies, D. L., Shepherd, M. *Lancet*, July 16, 1955, p. 117.
2. Folkson, A., May, A. R. *Brit. med. J.* Nov. 5, 1955, p. 1121.
3. Bein, H. J. *Ann. N.Y. Acad. Sci.* 1955, **61**, 4.
4. Bein, H. J. *Experientia*, 1953, **9**, 107.
5. Schneider, J. A. *Amer. J. Physiol.* 1955, **181**, 64.
6. Schneider, J. A., Plummer, A. J., Earl, A. E., Gaunt, R. *Ann. N.Y. Acad. Sci.* 1955, **61**, 17.
7. Chen, G., Ensor, C. R., Bohner, B. *Proc. Soc. exp. Biol., N.Y.* 1954, **86**, 507.
8. Rinaldi, F., Himwich, H. E. *Ann. N.Y. Acad. Sci.* 1955, **61**, 27.
9. Schneider, J. A., Earl, A. E. *Fed. Proc.* 1954, **13**, 130.
10. Monroe, R. R., Heath, R. G., Mickle, W. A., Miller, W. *Ann. N.Y. Acad. Sci.* 1955, **61**, 56.
11. Jenkner, F. L., Ward, A. *Arch. Neurol. Psychiat.* 1953, **70**, 489.
12. Zimmerman, F. T., Burgemeister, B. B. *Ann. N.Y. Acad. Sci.* 1955, **61**, 215.
13. Chen, G., Ensor, C. R. *Proc. Soc. exp. Biol., N.Y.* 1954, **87**, 602.
14. See *Lancet*, Aug. 13, 1955, p. 330.
15. Tweedy, P. S. *Ibid*, July 30, 1955, p. 249.
16. Macarthur, J. G., Isaacs, B. *Ibid*, Aug. 13, 1955, p. 347.
17. Miller, J. C., Pryor, W. W., Gibbons, J. E., Orgain, E. S. *J. Amer. med. Ass.* 1955, **159**, 836.
18. Schroeder, H. A., Perry, H. M. *Ibid*, p. 839.
19. Achor, R. W. P., Hanson, N. D., Gifford, R. W. *Ibid*, p. 841.

# Annotations

## INCREASED GROWTH-RATES IN CHILDREN

ONE of the most consistent and astonishing biological trends of our time is the tendency to reach physical maturity earlier and earlier: children, it seems, are getting older every year. The age at first menstruation is the criterion of maturity which has been most thoroughly investigated, and the results of these studies, discussed in detail recently by Tanner,[1] leave no doubt that the age of menarche has advanced quite regularly in Western Europe and America for the last hundred years at the almost spectacular rate of four to six months per decade. The average age of menarche in Norway, for example, was about 17·0 in 1850; in 1950 it was 13·5, the same as in England at that time. The maturing process has accelerated at all ages, so that by the age of 5 children today are already much bigger than they were, say, twenty-five years ago. The Swedish data quoted by Tanner show that school-children measured in 1938 were the same size as children eighteen months older in 1883. American, Scandinavian, and British data all give secular trends of very similar magnitude—about 1·5 cm. and 1 lb. per decade at ages 5 to 7, increasing to about 2 cm. and 3 lb. per decade during adolescence.

The trend is still, it seems, in full swing, and the latest contribution to its study comes from the records of the London County Council.[2] This is a report of the heights and weights of a sample of 20,000 children aged 5 to 16, measured in 1954; these figures are compared with the corresponding ones for 1948 and show increases precisely consistent with the previous trend. The L.C.C. do admirably to plan a series of cross-section surveys of this sort from time to time, but they would be more valuable if the methods used were more in line with the newer standards of technique, as illustrated, for example, in the studies of Krogman.[3] In the L.C.C. survey, children were weighed in "ordinary indoor clothing but without footwear," but no indication is given of the weight of the clothes—though the weights were recorded to the nearest 0·1 kg. This procedure is justified on the grounds that this was what was done in 1948, and comparison with those results was the objective; but it would perhaps have been better to measure a sample of the children clothed and unclothed so that the change from one etchnique to another could have been made with accuracy. Heights were also measured, but in what way is not stated; the height-scales attached to most weighing machines are grossly inaccurate and never as satisfactory as the old book-on-the-head-standing-against-the-wall technique.

The L.C.C. investigators also asked the girls whether they had started to menstruate or not, but they did not treat the resulting data by the method of probits so as to obtain a valid figure for the average age of menarche. The figure they give, which is the age by which half of the girls interrogated had reached menarche, is 12·9 years, but this rather underestimates the mean, since the sample lacks an adequate number of those aged 15 and 16, and there were no older girls, some of whom must constitute the older end of the non-menstruating group. Nevertheless, the true average figure can scarcely be more than 13·25 years, and this figure receives some support from the very careful and extensive study of children's measurements recently reported by Provis and Ellis.[4] In a random sample of Edinburgh children of all social classes, they found a mean menarche age (by probit fitting) of 13·35 years. Furthermore, the Edinburgh children are lighter and shorter than London children at all ages from 5 to 14 and perhaps later (the sampling of both studies at older ages becomes suspect). The differences are quite considerable—roughly about 1 inch in height and 1 lb. in weight. It may be that London children are more mature than Edinburgh ones; or perhaps the final adult size is greater in London. Only studies of bone-age could distinguish these alternatives. However this may be, both the London and Edinburgh reports give further evidence that this trend is a real one. Choirmasters, we understand, were not in doubt, for they have for some time been finding it increasingly difficult to get enough soprano choirboys.

1. Tanner, J. M. Growth at Adolescence. Oxford, 1955.
2. Report on the Heights and Weights of School Pupils in the County of London in 1954. London County Council, 1955.
3. Krogman, W. M. *Monogr. Soc. Res. Child Develpm.* 1950, **13**, no. 3.
4. Provis, H. S., Ellis R. W. B. *Arch. Dis. Childh.* 1955, **30**, 328.

## IDIOPATHIC HYPERCALCÆMIA

IN 1952 Lightwood drew attention [1 2] to a disease of infants in which failure to thrive, vomiting, constipation, and hypotonia are associated with a raised serum-calcium level. The prognosis is fairly good, and it seems that these cases of "idiopathic hypercalcæmia" should be distinguished [3] from a more grave condition, described by Fanconi et al.,[4] in which serum-calcium is also raised, but in addition there is mental retardation, a particular facies, and osteosclerosis. In both conditions the mechanism by which the serum-calcium rises is obscure, but the resemblance between the milder disease and intoxication with vitamin D [5] was soon apparent.[6] Even the usual intake of vitamin D may be well above the ideal level; the optimum has been placed as low as 500 i.u. daily,[7] and artificially fed infants can easily be given too much in fortified foods and cod-liver oil. The response to vitamin D and the need for it probably do vary widely from oversensitivity [8] to resistance.[9] Furthermore, artificially fed infants may be getting a lot of calcium, because the cow's milk contains four times as much calcium as breast-milk.

Bonham Carter and his colleagues [10] have recently published observations, begun in 1952, which greatly help our understanding of the idiopathic hypercalcæmia of Lightwood. They studied a nine-month-old boy in whom the diagnosis was first suspected when a loud systolic murmur was heard. These murmurs have been heard in the more severe disease described by Fanconi et al.,[4] but it is clear that they may be present in the milder disease as well. Calcification of the valve cusps [11] has been given as an explanation. Bonham Carter et al. felt justified in finding out whether vitamin D did in fact influence the boy's condition—a matter of importance in deciding his subsequent treatment. For ten days, at a time when his disease was in remission, he was given 10,000 i.u. daily of vitamin D, and this made him worse. Although 10,000 units is a large dose for a child without rickets, one would not expect it to produce any ill effects in a normal child. They then gave him a constant diet containing very little vitamin D, and varied the calcium content of the diet from none at all to 610 mg. daily. On the calcium-free diet the plasma-calcium fell to normal and the boy's symptoms rapidly diminished; others have made the same observation.[12] On the diet containing calcium the plasma-calcium rose again and the symptoms returned. The boy absorbed an abnormally large propor-

1. Payne, W. W., Lightwood, R. *Arch. Dis. Childh.* 1952, **27**, 302.
2. Lightwood, R. *Arch. franç. Pédiat.* 1953, **10**, 190.
3. Lightwood, R., Stapleton, T. *Lancet*, 1953, **ii**, 255.
4. Fanconi, G., Girardet, P., Schlesinger, B., Butler, N., Black, J. *Helv. pædiat. acta*, 1952, **7**, 314.
5. Fanconi, G., de Chastonay, E. *Ibid*, 1950, **5**, suppl. 5.
6. See *Lancet*, 1954, **ii**, 127.
7. Woodcock, R. H. *Ibid*, p. 243.
8. Thatcher, L. *Ibid*, 1936, **i**, 20.
9. Jonxis, J. H. P. *Helv. pædiat. acta*, 1955, **10**, 245.
10. Bonham Carter, R. E., Dent, C. E., Fowler, D. I., Harper, C. M. *Arch. Dis. Childh.* 1955, **30**, 399.
11. *Helv. pædiat. acta*, 1955, **10**, 149.
12. Ferguson, A. W., McGowan, G. K. *Lancet*, 1954, **i**, 1272; *Ibid*, 1954, **ii**, 817.

tion of the dietary calcium from the gut and the urinary excretion of calcium was high. He was later given a small intake of vitamin D and calcium; and eventually he was able to tolerate a normal diet. What happened to the systolic murmur is not recorded. These findings make it very likely that an increased sensitivity to vitamin D, with consequent increased absorption of calcium from the gut, explains at least some of the cases of the milder disease.

Anderson et al.[13] described an abnormal sensitivity to vitamin $D_2^{\prime}$ in sarcoidosis, explaining the raised plasma-calcium sometimes encountered in this condition by excessive intestinal absorption. After cortisone the response to vitamin D became more normal. No-one has yet studied the absorption of calcium in infants with idiopathic hypercalcæmia treated with cortisone, but it may help them too by reducing calcium absorption, for some of these infants have improved on cortisone.[14 15]

There is still much to be learned about the disease, in particular to what extent an apparent sensitivity to vitamin D depends on the intake of calcium. Meanwhile, treatment with a diet low in calcium and vitamin D, quite apart from the possible use of cortisone, seems generally successful; and it is obviously important above all not to treat undiagnosed cases of "marasmus" with additional vitamin D on the assumption that there may be a lack of it: an excess is nowadays at least as likely.

## SPORADIC CRETINISM WITH GOITRE

CRETINISM with goitre is well known in areas where adult goitre is endemic. Elsewhere, cretins usually have atrophic thyroids, generally explained as a failure of development of the gland. But goitrous cretins are occasionally found in districts where the incidence of ordinary goitre is low. Several of these have now been intensively studied by means of radioactive iodine, with interesting results. In all the reported instances there was a definite tendency for several members of a family to be affected.

The results of these observations show that there are two distinct types of biochemical defect. There are the cases investigated by Stanbury in Boston[16–18]: here radio-iodine studies showed that the thyroid could scarcely metabolise iodide at all. It was concentrated in the thyroid in inorganic form and could be washed out of the gland by giving the patient thiocyanate. This type of defect may be explained as a failure of the enzyme which oxidises iodide to iodine and enables it to combine with protein in the form of diiodotyrosine radicles. Later these diiodotyrosine radicles may be presumed to fuse to form thyroxine. On the other hand, Stanbury and his associates[16–19] have also been investigating two further families of goitrous cretins—one in Boston, the other in Leiden. In these cases the thyroid rapidly oxidised and bound iodide, as shown by the failure of thiocyanate to reduce the radioactivity of the gland. Subsequently mono- and di-iodotyrosine were identified in the blood by chromatography, together with small quantities of thyroxine and tri-iodothyronine. The excised goitre also contained large amounts of mono- and di-iodotyrosine, but only a little thyroxine and tri-iodothyronine. In these cases it is clear that the first step in hormone synthesis is taken normally, for administered tracer iodide is freely oxidised and bound to protein in the form of iodinated tyrosine radicles. But these radicles it seems can be coupled only with difficulty, so that there is a deficiency of active hormones. It seems likely that the patients studied earlier by Hubble[20] in Derbyshire and McGirr and Hutchison in Glasgow[21] may belong to the same group.

The accumulated evidence allows us to suppose that two distinct biochemical defects can be found in the thyroid. The fact that these lesions are congenital and appear in families strongly suggests that they are genetically determined. The simplest hypothesis would be that the absence of a single gene is in each case associated with the absence of a single thyroid enzyme. It is to be hoped that more of these cases will be identified and studied in the hope of confirming this attractive explanation. At the same time, it must be said that these new observations do not alter the treatment of a cretin (goitrous or otherwise): thyroid extract must be started as soon as the diagnosis is made and continued throughout life with the minimum of interruption.

## MALADJUSTED CHILDREN

THE report[22] on maladjusted children which has just been issued by the Ministry of Education is an important and sympathetically written survey of the existing medical, social, and educational services available for unhappy and emotionally handicapped children. It covers all the services, and concludes with no less than 97 conclusions and recommendations for the future development and deployment of the various agencies and organisations at present seeking to cope with the problem.

Maladjustment is a concept with hazy definitions that has on occasion been used to connote eccentricity of outlook or oddness of behaviour. The report seeks to define it in relation to the normal, and a whole chapter is in fact devoted to a description of normal psychological development in childhood and adolescence. Normal behaviour is not always socially acceptable behaviour. It is behaviour that expresses developing independence and self-control, making for responsibility and decision as opposed to impulse and whim. It is, within limits, appropriate behaviour, falling within the norms, and relative to a particular pattern of cultural background. Maladjustment reveals itself by emotional insecurity, unhappiness (however masked by aggression and bravado), and failure in personal relationships and in habits of hard work and reliability. The maladjusted child is an unhappy and an inefficient child—a misfit.

Though the worst effects of maladjustment are seen in youth and later life, it is really a problem of infancy and childhood. The final answer is clearly to prevent it arising in childhood by making sure that children and all who have to deal with them are trained in the known principles of mental health. At the same time, steps must be taken to deal with emotional difficulties at the earliest possible stage. This is a task for school-teachers and parents, who should be able to detect symptoms of disturbance and know where to turn for guidance. Unfortunately there are at present all too few child-guidance clinics available for consultation and treatment. There are not enough special schools, either residential or day, and there are not enough psychiatrists or psychiatric social workers to staff new units. The report estimates that some 400 more psychiatric social workers are needed during the next ten years, together with 140 new psychiatrists to man the child-guidance service alone. If these are to be provided, more candidates of the right kind will have to be found and encouraged to undertake training. As Woodger[23] has lately re-emphasised, little time is given in most British medical schools to child or any other psychology. The

13. Anderson, J., Dent, C. E., Harper, C., Philpot, G. R. *Ibid*, 1954, ii, 720.
14. Creery, R. D. G., Neill, D. W. *Ibid*, p. 110.
15. Fanconi, G., Spahr, A. *Helv. pædiat. acta*, 1955, **10**, 156.
16. Stanbury, J. B., Hedge, A. N. *J. clin. Endocrin.* 1950, **10**, 1471.
17. Stanbury, J. B. *Ibid*, 1951, **11**, 740.
18. Stanbury, J. B., Ohela, K., Pitt-Rivers, R. *Ibid*, 1955, **15**, 54.
19. *Ibid*, p. 1216.
20. Hubble, D. *Lancet*, 1953, i, 1112.
21. McGirr, E. M., Hutchison, J. H. *Ibid*, p. 1117.
22. Report of the Committee on Maladjusted Children, H.M. Stationery Office. Pp. 180. 6*s*.
23. Woodger, J. H. *Lancet*, Aug. 27, 1955, p. 419.

medical student is seldom aware of the need for this work, or of the rich opportunities that await those who will do it, and the report recommends that all medical students should receive such instruction and should attend a child psychiatric department for practical training. All medical schools should have links with a child-guidance clinic. This is, of course, being done in a number of schools to very great advantage, and the practice, if extended and made universal, might go a long way to stimulating likely candidates to prepare themselves for a career in psychological medicine.

The report also has important things to say about the training of teachers and the development of antenatal and child-welfare centres in an all-out campaign to rouse public interest and teach the importance of mental health. In the main it concentrates on suggesting ways in which existing services could be adapted and expanded rather than recommending radical changes and the establishing of new services. The report illustrates the shift of emphasis in medicine from cure to prevention, and this involves a realisation that mental health is not merely the absence of mental illness. In encouraging this change of outlook, sociologists, educators, doctors, and parents can all help to promote the environment and attitudes of mind necessary for the healthy mental development of children.

## VITAMINS IN REVERSE

THE existence of antivitamins is now generally acknowledged. Even in 1948 enough was known of their action to provide material for an international conference, which was held at Lyons. Subsequent research has revealed the importance of these substances in both the causation and the treatment of disease. The wealth of knowledge now at our disposal has been reviewed at a conference held in New York under the auspices of the National Vitamin Foundation.[1]

An "antivitamin" may be defined as a physiologically inert or useless substance which chemically resembles a particular vitamin, and which can obstruct the vitamin by usurping its place in biochemical systems. On this basis the sulphonamide drugs are presumed to act by interfering with the metabolism of *p*-aminobenzoic acid—a disturbance which affects the invading bacteria more than the host. The insecticide gamma benzene hexachloride ('Gammexane') is held to compete with inositol, which has much the same structure but with the chlorine atoms replaced by hydroxyl groups. The same principle applies, however, not only to inhibitors of these two "pseudo" vitamins, but also to inhibitors of true vitamins, such as aneurine and riboflavine, and of substances which are not vitamins, such as methionine and purines. The concept of "antivitamins," therefore, merges into that of antimetabolites in general.

The action of vitamins may be opposed in other ways than by competition. Thus substances which in chemical structure do not resemble the vitamins may interfere by causing their destruction, or by acting in the reverse direction. One example is the destruction of vitamin $B_1$ by an enzyme present in raw fish, which has caused serious losses to American fur farms. A similar enzyme has been found responsible for "bracken poisoning" among farm stock in Wales. Rancid fats can cause the destruction of vitamins A and E, or may oppose their action, and so give rise to conditioned deficiencies of these vitamins.

At the New York meeting K. P. Link spoke on vitamin K and the 4-hydroxy-coumarin anticoagulants. In this field we have an example of vitamin inhibition which was first revealed by the hæmorrhagic symptoms produced in farm animals, but which was later successfully applied to the treatment of thrombosis. J. H. Burchenall discussed folic-acid antagonists, which have been used in the treatment of leukæmia in children. Considerable clinical benefits have been observed at the start of such therapy, but with the development of resistance to the antagonist the dose has eventually to be raised to a toxic level. W. W. Umbreit dealt with research on antagonists to vitamin $B_6$, which in R. S. Goodheart's opinion had led to the recognition of deficiency of this vitamin as the cause of a convulsive disorder in infants fed on a certain proprietary food. L. R. Cerecedo, J. P. Lambooy, O. D. Bird, and G. H. Hitchings reviewed antagonists to vitamin $B_1$, riboflavine, pantothenic acid, and purine derivatives.

A fascinating story was told by D. W. Wooley, who related canine hysteria to a disease of tobacco plants known as wildfire. The tobacco leaves become infected with *Pseudomonas tabaci*, which produces a toxin that causes wilting. Wooley isolated this toxin, and elucidated its constitution. For its first four carbon atoms its structure was the same as that of methionine, which is the substance in flour that produces the poisonous sulphoximine on treatment with agene. Wooley conceived that both the toxin and the sulphoximine may act as antimetabolites to methionine. In support of this view the sulphoximine was found to cause wilting when placed on tobacco-leaves, although less intensely than the natural toxin. In cultures of chlorella antagonism between the tobacco toxin and methionine was clearly shown, but methionine did not protect the wilting leaf. So far no evidence has been presented on the crucial question whether the wildfire toxin can produce hysteria in dogs.

Anti-vitamin-E stress factors, and their relation to lipid peroxides, were discussed by E. L. Hove. The vitamin-E antagonists, which cannot be regarded as antivitamins in the strict sense, include such widely assorted substances as unsaturated fats, *o*-cresyl esters, carbon tetrachloride, pyridine, sulphathiazole, and sodium sulphite. In contrast to the anti-oxidant activity of vitamin E, these antagonists act as pro-oxidants, and promote the formation of lipid peroxides in the tissues. The oxidised lipids are believed to cause the various pathological states associated with vitamin-E deficiency by reacting in turn on sulphydryl-sensitive enzyme systems; hence the liver necrosis in rats or pigs which have been given diets deficient both in the sulphur-containing cystine and in vitamin E. An alarming practical demonstration of vitamin-E antagonism in man was seen in an outbreak of "ginger paralysis" caused by drinking an alcoholic extract of Jamaican ginger root containing *o*-cresol.

The power of vitamin antagonists, both for good and for evil, has been amply confirmed. In this field great successes doubtless remain to be won, particularly through attacking diseases refractory to conventional methods of treatment.

1. *Amer. J. clin. Nutr.* 1955, 3, 271.

## HEROIN

BY his misgivings about the legality of their method of stopping any further manufacture of heroin in this country, Lord Jowitt has obliged the Government to confine their present action to prohibiting export of the drug. Even those of us who think that, because of this country's international obligations, the Government were right in deciding to ban the drug altogether must be glad that this decision cannot take effect immediately, at a time when so many people believe it to be wrong. With fuller information, and quiet discussion of the issues, there may well be more agreement on what ought to be done.

---

Dr. T. B. DAVIE, principal and vice-chancellor of the University of Cape Town, and formerly Holt professor of pathology in the University of Liverpool, died in London on Dec. 14 at the age of 60.

# Special Articles

## STRAINED RELATIONS

R. M. ELLISON
M.D. Edin., D.P.M.
CONSULTANT PSYCHIATRIST, HELLINGLY HOSPITAL, SUSSEX

"All adversity finds ease in complaining"
—ISIDORE, quoted by Robert Burton, *Anatomy of Melancholy*

THOSE treating the physically or mentally ill have long realised that the judicious management of the patient's relatives is important, particularly perhaps in hospitals. From the young sick child and his relatively young parents to the senile case and his relatively old children, this is true. Most relatives are coöperative and grateful, and appreciate all that the doctor tries to do—be it to heal, to relieve, or only to comfort.

It is right and proper that relatives who are not satisfied with the medical arrangements should have their complaints investigated and any defects remedied. Other than those with genuine grievances, however, there remain a few relatives who can never be satisfied, and are accorded a disproportionate amount of attention from the medical and nursing staff. What is the cause of this unwarranted dissatisfaction? I shall consider this question with special regard to patients in hospital, but much of what follows will apply also to patients who are being treated in their own homes.

The largest group of the dissatisfied is met among the relatives of chronic or senile patients, who do not need any special treatment but only constant care and attention. The relatives appreciate how little treatment is needed and is being given in hospital and they know that they themselves could provide it at home. Often this would be inconvenient and would impose on them many distasteful tasks. To convince themselves, the patient, and the medical staff of their love and solicitude, they feel compelled to be perpetually dissatisfied and critical of the treatment and the wards in the hospital. By their complaining they seek to prove their concern and interest; it is their way of doing something for the patient—compensating for the guilt they feel that the patient is in hospital and not being looked after by them at home. They believe that, in the eyes of the world, their interest in the patient's welfare will be in direct proportion to the agitation they cause when visiting the hospital.

The number of chronic and senile patients is increasing, largely because of man's greater expectation of life. Previously, with larger homes, bigger families, and more domestic help, these patients could be adequately cared for at home. With modern conditions of smaller houses and families, many of them today cannot be kept at home. But there still remain some who need not be in hospital, if the younger members of the family regarded their care as a duty. With the introduction of the National Health Service the unworthy but powerful deterrent of having to pay directly for a hospital bed has been removed. However, patients are happier and better treated in hospital than in a home where they are not wanted and made to feel a burden.

Another group of relatives who complain are those who feel that they are the cause of the patient's illness and that through their neglect or failure to summon medical help earlier, the patient became so ill as to need admission to hospital. Their feelings of guilt and frustration are expressed either as remorse or, taking a more active and outward form, as aggression towards the hospital authorities.

A third group of relatives adopt an aggressive attitude because they fear the disease or, what seems to them, inevitable death. Their aggression is an attempt to fight the illness in the one they love, or to ward it off from themselves.

In a family the stress of illness, especially a long one that needs admission to hospital, may put an emotional and financial strain on the relatives. As a result, they may develop an anxiety state of which tension and irritability may be the outstanding symptoms. Such symptoms may be exaggerated or less controlled when visiting the hospital and lead to discontented behaviour. In cases of mental illness this may be more obvious, for relatives of these patients may have an inherited mental instability, which makes adaption to environmental stress difficult.

SUMMARY

Among the relatives of patients, a small proportion are chronically and irrationally dissatisfied with the medical services provided; the main causes of their discontent are a compensatory aggression for feelings of guilt and frustration or a fear of the illness. Many relatives show symptoms of an anxiety state, while others are constitutionally mentally unstable.

Understanding of the causes of dissatisfaction may help to mollify the strained relations that sometimes exist between doctors and unhappy relatives.

## FURTHER HEALTH CENTRE IN ESSEX

OPENING a health centre on the Aveley Housing Estate at Thurrock, Essex, on Dec. 16, Mr. Iain Macleod, the Minister of Health, said that probably new towns and new estates would continue for some years to be the laboratory in which health-centre experiments would be devised and observed. He went on to say that probably we can look forward to no large increase of health centres in the near future; but meanwhile we should be gaining knowledge of their working, learning to improve them, and perhaps learning lessons that could be applied in other fields. Mr. Macleod pointed out that health centres did not provide new services: they brought together services that otherwise would be separately housed. Almost all the services that could go into a centre existed separately in some degree in most areas. "The health service can never afford and probably will never be able to afford to pull down what is already good in order to put up something that is perhaps only a little better." Even if that were economic it would not be possible to bring about arbitrarily a change in the local customs and practices of the patients and of the professions which served them. Mr. Macleod hoped that as time went on there would be more experiments in different parts of the country. If there were to be more it would be because local people wanted them.

The Aveley Estate, covering 1200 acres, is being developed as a result of a decision by London County Council in 1947, in accordance with the Greater London plan put forward by Sir Patrick Abercrombie in 1944 to deal with the problems arising from the increasing population of the London area. The cost of development is estimated at nearly £9 million, and allowance has been made for over 5000 houses and flats, which are now nearly all completed. A special group of single-storey dwellings, together with recreation-rooms, has been built for old people.

The new health centre is generally similar to Essex County Council's first centre at Harold Hill [1]; but several minor improvements have been incorporated. As at Harold Hill the building consists of a two-storey wing on the main frontage with a single-storey wing running towards the rear. There are two entrances on the main frontage. One of these entrances leads to the rooms occupied by the general medical services, which make up a self-contained unit occupying the whole of the ground-floor of this wing. This suite of rooms includes four consulting-rooms with examination-rooms, waiting-

1. See *Lancet* 1954, ii, 866.

rooms, a minor-operations room, a clinical side-room, and a small inquiry office where the main telephone switchboard has been placed. The other entrance on the main frontage leads to the part of the building occupied by the county-council's clinic services, the regional hospital board's specialist services, and the general dental services.

To the right of the clinic entrance is a pram shelter, which has a separate covered access to the main vestibule, where the inquiry office is situated, and to the waiting-hall, where provision is made for the sale of welfare foods and the supply of light refreshments to those attending the centre. The remainder of the single-storey wing is taken up by a minor-ailments clinic, weighing-room, consulting-room, dressing-rooms, a large orthopædic room, and a kitchen. On the first floor, over the general medical services wing, are a health-visitors' room, an eye-testing room, a second waiting-room, and the dental suite comprising two dental surgeries, recovery-room, dark-room, and dental workshop. There is also a caretaker's flat on this floor.

## KING EDWARD'S HOSPITAL FUND

PRESIDING over the general council of King Edward's Hospital Fund for London on Dec. 14, the Duke of GLOUCESTER referred to the Hospital Administrative Staff College established by the Fund, and he said it was hoped that a Government scheme would shortly be launched for the selective recruitment and training of hospital administrative staff on a national basis. The intention would be to help to provide the hospital service with well-trained administrators who would be competent to fill the senior administrative posts in years to come. The Fund's staff college was expected to play an important part in the training of these student administrators, who would be selected from promising younger officers in the hospital service and from university graduates and other entrants with professional qualifications. Subject to the consideration of certain points still to be settled, the Fund would be happy to use the resources of the Hospital Administrative Staff College to assist the scheme, and the Duke felt confident that the college would be able to play a useful part in the light of the experience it had gained since it was opened in 1951.

Dr. G. F. ABERCROMBIE, chairman of the Emergency Bed Service committee, traced the development of the service since the time, in 1938, when general practitioners in London received a neat card to say that if they would ring a certain number and give details, a new department of the King's Fund would help them to get their urgent cases into hospital. The idea was so successful that, ten years later, the service was dealing with about 13,000 applications a year. Today it was open day and night and it dealt with its 500,000th application last January; it expected to receive about 65,000 applications each year.

Eighteen months ago, the head office and its four outlying branches were brought together in specially designed accommodation in Fielden House, London Bridge Street. On an average it took 27 minutes to see a successful admission through from the general practitioner's call to the E.B.S.'s request for an ambulance. In summer the weekly total of requests was below 800, but in winter, and particularly during an epidemic, the total would be twice or even three times that of summer, and, as the hospitals filled, the admission-rate tended to fall.

The E.B.S. had two methods of meeting crises. Firstly, any individual patient for whom no bed could be found might be submitted, through a medical officer appointed by the regional hospital boards, to the medical referee of that patient's hospital management committee, for immediate admission. Dr. Abercrombie emphasised that every patient, represented as in urgent need of treatment which could be obtained only in hospital, was admitted. Secondly, there was an elaborate warning system, calculated from the weekly total and based upon the percentage of success in securing beds. If this fell below 85% a white warning was sent to all hospitals. This said in effect: "E.B.S. is hard pressed, and may be in serious difficulties in a day or two." If success fell below 80% the warning was yellow, and if below 75% red. These were urgent calls for help and meant: "The situation *is* serious. The resources of the service are rapidly being exhausted, and for one patient in five—or even for one in four—no bed can be found." On receipt of these warnings, hospitals took their pre-arranged action to provide more beds, and as a result of this coöperation, the admission-rate had not fallen below 80% since the influenza epidemic in February, 1953.

The Emergency Bed Service, originally designed simply to save the time of the busy general practitioner, and to direct his patient to an appropriate hospital, had now become, Dr. Abercombie declared, an absolutely indispensable link between the two great partners in the medical service of the city. Moreover, the changing weekly total was considered by experts at the Ministry of Health to be the most sensitive index they had of the rise or fall of sickness among the people of London, and so the Emergency Bed Service had acquired a new function—namely, to give the medical administrator timely warning of trouble ahead.

Sir ARCHIBALD GRAY, chairman of the distribution committee, referred to the Fund's system of hospital visiting. When the National Health Service began, the Fund's maintenance grants ceased, except to a few disclaimed hospitals, and annual visiting also ceased. It soon became evident, however, that any help the Fund could give to hospitals, including visits, would be welcomed. The number of hospitals on the Fund's list had almost doubled, and it was clear that they would have to be visited as groups and not as individual hospitals. Already some 60 groups and teaching hospitals had been visited, and the remainder would be visited in the coming year. The visits were of great value to the Fund in keeping in touch with the progress of hospital development.

## TRAINING THE DISTRICT NURSE

THE annual meeting of the Queen's Institute of District Nursing was held in London on Nov. 29. Discussing the report of the Working Party on the Training of District Nurses.[1] Mr. A. H. M. WEDDERBURN, chairman of the general executive committee, explained that there was general agreement among the working party about the content of district-nurse training—and the content agreed was identical with the existing Queen's Institute syllabus and practice. There were, however, three main points of difference between the majority and the minority reports:

1. The majority believed that the training could be given in four months to state-registered nurses and three months to S.R.N.s with certain additional qualifications, while the minority view was that not less than six and four months respectively were needed.

2. The minority did not think that the proposed central committee should be obliged to issue a syllabus for the four-month and three-month periods, no more and no less. They believed these shorter periods, if adopted at all, should be a minimum training, thus conforming to all other branches of nursing training.

3. The minority pointed out that, despite its important functions, this central committee might very easily have on it not even one professional distruct-nurse training expert if the composition suggested by the majority report were adopted.

Why did the majority of the working party insist on cutting down the training period? How could a syllabus be devised which would carry out what they recommended? Mr. Wedderburn invited answers to these questions, but no-one from the audience of more than 500 spoke in support of the majority report.

Dr. E. C. H. HUDDY, county medical officer of health for Berkshire, thought that the majority report was against the weight of evidence, against the opinion of

1. See *Lancet*, Sept. 10, 1955, p. 543.

the nurses concerned, and against the opinion of most general practitioners.

Dr. GEOFFREY HALE held that the majority report showed little appreciation of the difference between district nursing and hospital nursing. The technique and the approach were very different, and the differences took time to learn and to practise. It was remarkable that the basic six months' district-nurse training had not been increased over the years, and, as a general practitioner, he would not be confident that his patients were properly cared for if the district-nurse training were not at least as long as at present.

Mrs. HENRY BROOKE said that, owing to the increasing cost of hospital beds, a more speedy discharge of patients from hospital was desirable, and it was therefore very important that the nursing care in their own homes should be of the very best.

## Points of View

### REMEMBERING AND FORGETTING

ALAN MCGLASHAN
M.C., B.A. Camb., M.R.C.S., D.P.M.

MEMORY, the psychologists briskly tell us, has two main aspects. The first is reproduction—not necessarily exact, as they concede with the naïveté which is the birthright of academic psychologists. The second is recognition—that rainbow bridge flung in a magical instant between the present and the past. Recognition is the core of memory and of mental life. Without it nothing could be experienced, neither love nor hate, hope nor fear, beauty nor ugliness; and a merely vegetative existence would remain. Hardly even this perhaps; for as the physical world is held in being by the all-pervasive, unobtrusive force of friction, so without remembering the entire architecture of the psychic world might disintegrate. Memory is, in fact, the mortar between all events—a veritable *glutinum mundi*.

This basic function apart, memory has other and more equivocal uses. It is, for instance, the guardian of self-love, interposing between past and present an invisible web, through which only selected and fondly edited items can pass into the specious records of the conscious mind. Memory has its graces too, storing sharp images of happiness and grief, laying a soft patina on the past, giving to the unripe act of living what autumn's gold gives to the mellowing peach.

But if remembering is a vital function, so also is forgetting. To forget is essential to sanity. Recalled in their entirety, the huge inchoate body of past events would suffocate our mental life. If all things were clearly remembered, experience would lack its chiaroscuro, and history's canvas would have the maddening facial iteration of a mammoth end-of-term school photograph. Man owes more than he guesses to oblivion. Through forgetting comes much beauty into life, much richness and strangeness.

* * *

Since man must remember if he is not to become meaningless, and must forget if he is not to go mad, what shall he do? The dilemma, not logically resolvable, has been subtly resolved. Within man the past is perfectly contained—but he is allowed to live as if it were lost. He is tolerantly permitted to taste a naïve pride of discovery: as when William Harvey staggered the 17th-century world by his discovery of the circulation of the blood—in which he had been anticipated by Hwang Ti, Emperor of China in 2650 B.C., who noted that "all the blood in the body is under the control of the heart . . . the blood current flows continuously in a circle and never stops."

Yet the pristine forms of knowledge are not wholly forgotten. Mixed always with the joy of new discovery is a shadow of disquiet, a teasing half-recollection of things long past—the secret penetration of the archaic into the present, of the timeless into the temporal. To the percepts of the conscious mind are added intimations from a distant and forgotten past, still alive in the depths of the psyche. Nowhere is this more clear than in our enjoyment of myth and parable and fairy-tale. Good stories are very rare, and these are the three forms in which they are most often contained. The best of them have indeed been told countless times through history and prehistory. This would be intolerable were it not for the grace of half-forgetting, as children do, which allows us to receive with a fresh delight tales first heard, perhaps, in some lake village of the Neolithic age. Like fascinated children, open-mouthed and a little frightened, we listen to our songs and stories echoing faintly back from the walls of eternity.

The tragedy is that it is fatally easy to lose the precarious balance of these opposing and compensating functions of remembering and forgetting, whereby the imaginations of men are grouped and regrouped, in endless intricate patterns of wisdom and folly, kindness and cruelty, insight and illusion. It is so hard to grasp this reciprocal movement, which alone creates the lovely iridescence on the surface of life, the fathomless quality in its depth. Genius has sometimes known this, and to see life *sub specie aeternitatis* is no new thing. In his book *Cumaean Gates* Jackson Knight suggested that the essence of genius "consists in the power to find contacts further back in time beyond the reach of others, and to evoke latent stores of feeling and of meaning in the collective mind of the present."

* * *

Genius is not the only guide. The evidence abounds, for it is inherent in all things. Even in the daily paper, that faithful mirror of disintegrated existence, faint intimations can be caught by an attentive ear. From what distant sources, and through what indefinable media, have lingered on such bucolic fancies, as that fresh earth from the grave of a baptised infant will make the blossoms of a plant larger and more handsome; that the cuckoo changes into a hawk at the end of summer; that driving rusty nails into a barren apple-tree will cause it to bear fruit? All these, with many more, have been seriously advanced within the last two years by correspondents to the English national newspapers.

There is a type of mind, otherwise intelligent, that reacts with a sort of snorting fury to these naïve beliefs, that feels outraged if they are not instantly dismissed with an impatient shrug. For many purposes, of course, they must be so dismissed: science has built its high-roads of fact and reason only by resolutely ignoring the wayward blossoms of the countryside. But life is so constructed that resolutely to ignore a thing is to ensure being eventually tripped up by it. One of the gayest, saddest sights on earth is to see the good nag Rosinante, carrying the scientific world on its back and confidently cantering along to its ultimate *quod erat demonstrandum*, suddenly put its foot in a *quod est absurdum*, and throw its illustrious burden: gay, because it is pleasant to see the rationalist with his heels higher than his fastidious nose for once; and sad, because he learns so little from his tumble.

In medicine alone there have been many such embarrassing faux pas. Not so long ago the doctors were loftily amused to hear of an old country-woman who used to treat dropsy with decoctions of foxglove from her garden—and who was finally proved to have been dispensing a hitherto unknown drug called digitalis. And only yesterday the mould on damp cheeses, kept in many a farmhouse scullery in our great-grandfathers' time to make a rude plaster for infected wounds, was shown to be the source of penicillin. In the country they know that things are only half-discovered—and half-remembered. The precarious balance is unconsciously preserved, and with it the secret of the crude sanity of country life.

Yet the scientific mind blandly ignores these constant exposures of its own limitations. Like Theseus, it "never may believe these antique fables, nor these fairy toys." Random proof, however startling, of the practical wisdom hidden in simple hearts seems only to serve as the origin of fresh distortions. With indecent haste the thought is separated, fatally, from the feeling that was its partner, and from the human context in which they quietly coexisted.

For the essence of this earthy wisdom lies precisely in its slow, centuried synthesis of thinking with feeling, of remembering with forgetting. It cannot be invented or new-minted from any single mind, but forms itself mysteriously, with the imperceptible accretions of a stalactite, in the ombrous caverns of the collective mind. And we do wrong if we dismiss this process as merely passive. Such silent, patient waiting for truth, as Simone Weil has said, is an activity more intense than any searching.

The products of this activity are unlike the clear concepts of the classroom and the laboratory. It is neither difficult nor clever to prove them logically absurd. In any case, being a human process, it is as fallible as all things human. But empty of value as many of these country tales undoubtedly are, childishly ridiculous as they all appear, they deserve gentle and perceptive handling, in virtue of the mystery of their origin. They belong not to the everyday world, but to the timeless paradoxical world of myth and fairy-tale, of fantasy and dream; a world where startling absurdities and glaring inconsistencies are but secret signals to the instructed mind, bidding it note the crossing of an invisible frontier.

* * *

It would be well if man could recapture this richer, older mode of response to existence, wholly lost to us these last three hundred years, which recognised that the final secrets of life may often be reached less by what we learn than by what we half-remember. What is needed is an extension of contemporary consciousness to include what can perhaps be defined as the translucent quality in all things—the quality by which an object or an event is seen not only as a thing-in-itself, but also as a membrane through which can dimly be discerned the stirring of a different order of experience.

This once caught, even for a moment, transforms the sensible universe, investing all objects with a sharp intensity of being. The seeming-solid world grows permeable, beginning to transmit, not merely to reflect, the light. The quality of translucence is the key; a golden key that is the careless plaything of all children, and the conscious instrument of a few geniuses. In exceptional moments of their lives ordinary men and women may fleetingly hold it: in the first days of overwhelming love, in moments of overwhelming peril, in the presence of new life, and sometimes on the unheralded news of death.

At such moments a man stands on tiptoe, and may catch a startled glimpse of another level of being, where all values are changed, and everything is understood differently; the level of which Chekhov dreamed where "everything is forgiven, and it would be strange not to forgive"; that Goethe experienced when he murmured to his friend "That fig-tree, this little snake, the cocoon on my window-sill quietly awaiting its future—all these are momentous signatures"; the level touched in the Parables, in the sixth book of the *Aeneid*, in the *Ode to a Nightingale*, and anonymously, and perhaps incomparably, in the mysterious golden light that shines through myth and fairy tale; the level of the kingdom of heaven that is within. It is a quality often missing in works of loftiest genius. Milton, for all the splendour of his planned achievement, and all the wealth of his well-chosen mythological themes, had not a trace of it; nor Shelley, despite his earnest preoccupation with eternity.

To become aware of this translucent quality in all things is no vague romantic goal. It is a sharply defined, delicately poised effort of mental vision, a state of harmonious balance of forces in the Pythagorean sense, born of the union of many opposites: of remembering with forgetting, of thinking with feeling, of the temporal with the eternal, of personal conscious perceptions with faint echoes from the remotest regions of the archaic psyche. It is the basis of all true science, the essence of ritual, the constant attribute of wisdom. It may be the nearest that human minds can reach to the meaning of meaning.

# Parliament

## Heroin Ban Postponed

IN the House of Lords on Dec. 13 EARL JOWITT moved:

That in the opinion of this House, in view of the apparent conflict of expert medical opinion on the banning of the manufacture of heroin in this country, the period of the present licences to manufacture should be extended pending the institution of further inquiries.

He fully realised that the Government had propounded the ban on the manufacture of heroin from the highest motives, but he thought that a pronouncement by the House of Lords might help to retrieve what he believed to be a grievous mistake. After summarising the circumstances which had led to the ban, and the medical advice which had, and had not, been sought he thankfully left what he described as "the sea of medicine" for an island of the firm ground of the law. There was, he suggested (and did not think the Lord Chancellor would disagree), serious reason to doubt whether the Minister had any right to use his powers under the Dangerous Drugs Act to ban the manufacture of heroin.

### CONTROL OR PROHIBITION

The granting of licences for the manufacture of heroin was, he thought, an incident to the general power of controlling manufacture; and the power to control manufacture was for the purpose of preventing the improper use of heroin. The Home Secretary had in effect said: "No particular individual can manufacture heroin unless he is licensed to do so. Therefore, if I announce in advance that I shall license nobody, I can indirectly ban the manufacture of heroin." The control of manufacture as a means of preventing improper use could be compared, Lord Jowitt suggested, to the control of a horse or a dog, or a child, by shooting it through the heart.

He maintained that the Home Secretary's action was outside his powers, and he begged the Government to consider the position. If they intended, for the first time, to ban a drug which many doctors thought to be of the first importance, this ought to have been done by a Bill and not by the indirect method of trying to use the Dangerous Drugs Act. The Minister should be scrupulously careful not to take a step which the courts might declare to be outside the law. If there could be no restraint through the courts this would be a good matter to refer to the Committee on Ministerial Powers which was now sitting.

### A CONTROLLED INQUIRY

Lord Jowitt then left his "little rock" and plunged again into the ocean of medical details. Having spoken of the weight of opinion against the ban he said that if the Government were going to incur the responsibility of banning heroin they must, in his view, show who was going to gain. They must, for instance, explain how it would avoid the problem in the United States. In the six years 1946–51 the total of illicit heroin seized in Britain was 11 grammes. In the rest of Europe in 1951 62,711 grammes were seized, and in North America 28,870 grammes. He asked the Government to postpone the ban and constitute an ad-hoc committee of eminent doctors to see whether the conflict could be resolved.

Lord MANCROFT, under-secretary of State for the Home Department, said that the Government would have to

look carefully at the legal point Earl Jowitt had raised. He agreed that there was no serious addiction problem in this country, but there was such a problem in other countries. Most addicts got heroin through the black market which was international. A few months ago three large seizures of heroin, amounting to over 80 lb. of the drug (enough for 2,250,000 doses), were made in American and Canadian ports. It was the considered view of all these countries that the difficulty of controlling the illicit traffic was increased by the existence of lawful manufacture and trade such as our own. If the manufacture of heroin were made illegal the task of suppressing the illicit traffic would be made much easier. Only 4 countries now opposed the ban. More than 50 countries had banned the use of heroin and in all of them the doctors had found satisfactory substitutes for use in medical practice. Without the assurance that the substitutes were reliable the Government would never have taken the decision to impose a ban. We were the largest manufacturer of heroin and were we not to agree with the United Nations' request to ban heroin we should lay ourselves open to the charge that we disregarded the fine example we had set in the past and had obstructed international measures to stamp out the traffic.

The restriction, he added, would not mean that supplies would cease as soon as the ban became effective. Stocks were sufficient almost for two or three years at the present rate of consumption and the interim period would give doctors an opportunity to gain experience in the use of alternative drugs. The Government would keep the restriction under searching review.

Lord MORAN believed that the Minister of Health had been unfairly criticised. He had consulted the only body which was set up by statute to advise him, and he could not have done anything else. If the Minister's professional advisers who earlier supported the ban now led a crusade against it, surely there must be an end of all confidence between the Minister and his advisers. It was upon the smooth working between the two that so much of the efficiency of the National Health Service depended.

From the division of medical opinion it was obvious how difficult it was to say whether there was an adequate substitute for heroin. There were almost insuperable difficulties in the way of a controlled inquiry. Indeed the measurement of pain almost defied an inquiry of this kind. What was the scientific value of the letters in the *Times*? They said, what we already knew, that heroin is an effective drug, but they did not compare it with other combinations of drugs and in that sense their observations were uncontrolled. Again some of the letters seemed to Lord Moran emotional rather than scientific. The doctor who was deprived of a drug was naturally aggrieved: he was even more aggrieved when he attributed this deprivation to the Minister of Health who, he thought, should not come between him and his patient. To this attitude of mind Lord Moran added the influence of habit. If a drug was effective, the doctor was inclined to go on using it to the exclusion of others.

But if a controlled inquiry was difficult, and if expressions of opinion were not real comparisons, was there nothing else to help us? Lord Moran suggested that there was a great deal of circumstantial evidence at our disposal. In the 54 countries where heroin was banned the doctors seemed to get on quite well without it, and to a certain extent it appeared that substitutes had been found satisfactory. A former president of the American Medical Association had cabled him

"American experience—nobody objects to ban on heroin except the addicts. Medical substitutes entirely satisfactory."

Again there were many hospitals in this country where heroin was used sparingly. The average consumption of heroin in ten teaching hospitals in 1953 was 432 grains. In a debate at the Royal Society of Medicine on the treatment of inoperable cancer, heroin was not mentioned. There were important textbooks, in common use by students, in which heroin was not mentioned. We should not ignore this body of evidence from those who did not use heroin.

Turning to another point, Lord Moran said that nobody would interfere between a patient and his doctor without good reason, but surely this freedom of the doctor could never be absolute. Surely we must not push a principle beyond the point of common sense. Surely the freedom of a doctor carried with it also responsibilities and some recognition of what was due to the community. For centuries we in this country had lived an isolated, happy life, enjoying the benefits of national sovereignty. The hydrogen bomb had put an end to that. We were faced in the future with grim alternatives. Anybody could see that there was no hope in the world unless there could be a measure of understanding among the nations—some degree of common action. Lord Moran asked the House to take a step towards that goal, and to make a contribution, however small, to the far-off ideal of the brotherhood of nations.

### ENGLISH METHODS

Lord WEBB-JOHNSON maintained that the Government had not yet had expert advice on the value of heroin as a therapeutic agent. He took the opportunity to point out that provision was included in the National Health Service Act to prevent the Central Council and the Advisory Committee from being used as supreme bodies for giving advice on medical matters. It was foreseen that the representative bodies of the profession might be short-circuited and ultimately superseded. If the British Medical Association and the Royal Colleges were to be supplanted, and if advice on medicine in general was to be sought from the Ministry's standing medical advisory committee, serious notice must be taken by the profession of the improper use of that committee. Meantime, he suggested that such advice as had been given and received might be withdrawn until consultations had been held with those who had the necessary experience to qualify them to advise. In future the advisory committee would be wise to refuse to advise on matters which ought to be referred to representative bodies of the profession, while in matters which required expert investigation they should appoint a subcommittee to report. We in this country had been wonderfully successful in preventing addiction to habit-forming drugs. Let other countries follow our methods. Should not other countries sometimes follow Britain? But do not let us follow along the path of prohibition—a bad and dangerous way, the tragedy of which he saw with horror.

Lord WAVERLEY had always regarded medical practice as a highly individual activity, and for a Government to deprive an able, responsible, and conscientious medical man of the opportunity of prescribing what he genuinely believed was necessary in the best interests of his patient was, in his view, indefensible in the absence of the most cogent and compelling reasons. He wondered what possible good the prohibition of the manufacture of heroin in this country was going to do to any other country. The proper course, he suggested, would be to prohibit the export of heroin and accompany that prohibition by the most complete control of manufacture.

Lord HADEN-GUEST, on the other hand, held that a narrow view must not be taken just because heroin addiction was not a problem in this country. For many years, fed by widespread international illicit traffic, it had been a grave social danger in the United States and Canada. It was the United States which was asking us now to join her in making this a universal ban. The struggle against narcotic drugs was an international problem and could not be solved at the national level. Lord AMULREE regretted that the Minister had not gone back to the Standing Medical Advisory Committee after he had received the deputation from the B.M.A. in July so that the committee could consider the objections.

### THE GOVERNMENT'S REPLY

Viscount WOOLTON, Chancellor of the Duchy of Lancaster, replying to the debate, pointed out that the medical committee which advised the Government consisted of people of extraordinary diversity. In it there was a great central body of opinion of the Royal Colleges, the General Medical Council, the British Medical Association, and from these people they had received a clear answer. He doubted whether clinical experiments on the use of heroin would be useful. It was difficult to prove a negative. They would be trying to prove that they could do without heroin, and surely the real

difficulty was that pain was not a measureable thing. But if the House thought that it would be a good thing, the Government were prepared to take early advice from the Medical Research Council as to whether it would be practicable to arrange a special series of scientific trials. But surely there was some clinical evidence on which they could form some judgment. There were many doctors in the country who did not use heroin, which suggested that other drugs could be effective.

He thought that in medicine during the past few years there had grown up a body of people who thought it necessary in the interest of their profession, to seek to protect themselves against incursion by the State into their affairs. But when an individual found himself opposed to the scientific thought of his profession Lord Woolton could not admit that he should be left as a law to himself. Prescription was obviously the duty of the doctor; but permission to trade in dangerous goods was the duty of the Government. The two factors must be balanced.

On the legal issue raised by Lord Jowitt, Lord Woolton suggested that the House would be well advised to suspend judgment until the publication of the Government's white-paper. Meanwhile he could say that the ban on heroin would not be imposed by the Government unless and until it was clearly established that such action could be legally taken. In order to give ample time for full and careful consideration on this matter the Government would not impose the ban on Dec. 31. Of course it would be for the Government to consider what the next step should be if the legal issue put forward by Lord Jowitt proved to be well founded.

After some discussion the MARQUESS of SALISBURY gave Lord Jowitt an assurance that licences for manufacture would be granted for the year 1956.

In announcing the postponement of the ban in the House of Commons on Dec. 16, Major GWILYM LLOYD-GEORGE, the Home Secretary, said that the only doubt that had arisen was on the legality of prohibiting manufacture of the drug. There was no doubt about the power to prohibit its import or export and no licences to import or export would be issued after Dec. 31.

Sir ROBERT BOOTHBY: Will the Home Secretary give an assurance that before any final decision is taken he will have further consultation with the B.M.A. and the M.R.C., and that the House will be given an opportunity of debating the subject?—Major LLOYD-GEORGE: It is not going to be easy to find something better than a representative committee to give advice to Ministers. We cannot consult the whole medical profession, and it is not a profession from which you get complete unanimity. But the point is surely that it is accepted on all sides that the proper bodies to confer on technical matters with the Minister are those representative of the particular profession or industry with which they have to deal. Otherwise consultation is utterly impossible. This committee has given two Ministers of Health advice on this matter, and I still cannot see what better representative committee one could get.

Dr. REGINALD BENNETT: Under his powers can the Home Secretary restrict the amount produced in the coming year to that needed here by the profession, taking account of existing stocks?—Major LLOYD-GEORGE: Yes.

## QUESTION TIME

### Single-handed Practices

In answer to a question Miss PATRICIA HORNSBY-SMITH, parliamentary secretary to the Ministry of Health, said that 230 single practices fell vacant during 1954, and 134 of these were filled on the same basis.

### Deaths from Pulmonary Tuberculosis

In answer to questions Mr. IAIN MACLEOD said that the number of deaths from respiratory tuberculosis in England and Wales fell from 19,088 in 1948 to 7069 in 1954.

### Student Mental Nurses

In answer to a question Mr. MACLEOD said that the rate of wastage of student mental nurses was estimated, in an investigation covering the years 1948 to 1953, to be about 60%.

### Drunkenness among Young People

Replying to a question, Major LLOYD-GEORGE said that in 1954 there were 124 convictions for drunkenness among 865,000 males, and 12 offences among 839,000 females, under seventeen; and 3157 offences among 1,041,000 males aged seventeen and under twenty-one, and 209 offences among 1,107,000 females aged seventeen and under twenty-one. The police, he was informed, had no reason to think that the figures indicated any tendency for juvenile drunkenness to assume serious proportions.

# Medicine and the Law

### Attempted Suicide not a Serious Crime

A 36-year-old labourer was seen by a police constable to steal a spare wheel and tyre from a motor van. He was arrested, and that night in his cell he broke the window, cut his neck on both sides with the glass, and called the gaoler. He was convicted of larceny and attempted suicide and, as he had a large number of previous convictions for various offences, including many for drunkenness, the magistrate who convicted him sent him to Stoke-on-Trent borough quarter sessions for sentence. At quarter sessions, while a probation officer was giving evidence, the recorder intervened and said: "May I be allowed to put the problem as it presents itself to me? Self-murder is one of the most serious crimes in our calendar. An attempt thereat, therefore, is a very serious crime indeed." He went on to say that he was minded to treat the attempt as a frivolous one but that the evidence had proved that it was a serious, sane attempt on the part of this labourer to take his life; how could he take that lightly? The recorder imposed sentences of two years' imprisonment for the larceny and two years' imprisonment for the attempted suicide, to run consecutively. The labourer appealed against the latter sentence.

The LORD CHIEF JUSTICE, giving the judgment of the court, said that never in his life had he heard of a sentence of two years' imprisonment for attempted suicide. The labourer was obviously of a somewhat unstable disposition; there seemed to have been some doubt whether his attempt was serious or not, though the doctor thought that it might have been a genuine attempt at suicide and not a piece of exhibitionism. It would not be right to say that attempted suicide was a trivial thing, but these attempts were made by unbalanced people. It was the first time that his Lordship had heard that suicide was one of the most serious offences known, and that attempted suicide was a very serious crime indeed. Suicide had been regarded by the spiritual courts as a crime and had been made a crime at common law to enable the Crown in the old days to obtain forfeiture of the suicide's goods, since anyone who committed suicide was supposed to have committed murder. Therefore it was a source of revenue to the Crown but it was not a very serious crime and to say that it was showed a lack of proportion. A short sentence was often imposed by the courts to protect a man against himself. Nowadays prosecutions for attempted suicide were rare and it was absurd to say that a sentence of two years' imprisonment ought to be passed. The court could not possibly allow such a sentence to stand and would substitute a nominal one of one month's imprisonment to run concurrently with the other sentence, against which no appeal had been made, of two years' imprisonment for larceny.

Regina *v.* French—*Court of Criminal Appeal:* Lord Goddard C.J., Hallett and Pearson JJ.: Dec. 12, 1955.

E. M. WELLWOOD
Barrister-at-Law.

### Hospital-authority Documents

There has been an unexpected sequel to a case in which the St. Albans coroner wrote to the Mid Herts Group Hospital Management Committee recommending an inquiry into the medical treatment of a woman who was admitted to hospital with aspirin poisoning and who subsequently died.[1]

The management committee adopted a report of the medical advisory committee[1]; and the gist of the

1. See *Lancet*, Nov. 26, 1955, p. 1132.

report was conveyed to the coroner in a letter from the secretary of the management committee. This summary was perhaps rather terse. At all events, the coroner did not see the full observations until he saw them reprinted, together with his own letter, in a local newspaper.[2]

The coroner thereupon wrote to the management committee complaining that they had not sought his permission to give his letter to the press. "Quite apart from breach of copyright," wrote the coroner, "I should have thought that if you wished my letter published, you would at least have had the common courtesy to ask me first, or at the very least, inform me of your proposals." The secretary replied that the press had been present "as usual" at the meeting of the management committee. This provoked a lengthy reply from the coroner in which he said:

"What I complain of is that when I write you a letter drawing attention to certain matters which seem to me to require further examination from a medical aspect, you take it upon yourself without any prior reference to me to have a copy made and pass it to the Press with the agenda of your committee. What right have you to publish . . . correspondence without first obtaining the author's consent? To do so is an infringement of copyright . . ."

The coroner's claim that his letter was protected by copyright raises important issues. It is true that prima facie the author of any letter has the benefit of copyright since it is an "original literary work"; the fact that the letter may be quite worthless as literature is irrelevant. But it is by no means certain that copyright can be claimed for a letter written to a public body such as a hospital management committee. Regional boards and management committees exercise their functions on behalf of the Minister of Health, and it may therefore be that in matters of copyright they have the privileges of a Government department. Even if a management committee does not have these privileges, there is a further consideration to be taken into account: it is customary (though not obligatory) for management committees to invite the press to their meetings, and it may follow from this that anyone who writes a letter to a management committee gives an implied licence to the committee to allow the press to have it with the agenda.

In any event, it would surely be unfortunate if the advancement of purely technical claims to copyright were to discourage regional boards and management committees from inviting the press to their meetings.

## Doctor Acquitted on Abortion Charges

At the Old Bailey recently a 37-year-old doctor was acquitted on six charges of illegally using an instrument with intent to procure a miscarriage.[3]

In a statement to the police, the doctor is alleged to have said: "I have not made a business of this. My motives have been altruistic rather than selfish, but to some extent it has derived from the difficulty I have in supporting my family. I am confident that these women would not inform on me. I presume your informant is . . ."

One of the women concerned, Mrs. H, said that she saw the doctor at his surgery in 1953 when she was three months pregnant. The doctor asked her if she had brought any money. She gave him £15 and a further £10 when he had performed the operation. She had a miscarriage the following day. She could not remember telling the doctor that the only way out for her was to commit suicide, but she had contemplated suicide.

Miss W, a medical student, said that after she became pregnant she made an appointment to see the doctor at his surgery. An operation was performed for which she paid £25. She said that she could not remember whether she had told the doctor that her mind had got into a state in which she could not work or study. At the time she was upset and depressed.

Another woman, Mrs. W, said that the doctor performed an operation on her when she was four months pregnant, for which she paid £25. She was not very well at the time. One of her troubles was that her boy, aged 4, was very difficult to manage, and she also had a baby six months old.

2. *Herts Advertiser*, Nov. 18, 1955.
3. *Kentish Independent*, Dec. 2, 1955.

In his own evidence, the doctor said: "I formed the view in each of the cases before the court that it was necessary for the health, both physical and mental, of the patients that an operation should be performed."

The doctor was asked by defending counsel whether he had ever done any of these operations where he felt it was merely a case of the girl or woman wishing to get rid of the baby, and for no medical reason. The doctor replied: "There was always a medical reason which satisfied me that there was a valid reason from the medical point of view.

After considering their verdict for two hours, the jury found the doctor "Not guilty."

## Wrong Finger Amputated

Giving judgment for the plaintiff in an action for negligence against the Birmingham Regional Hospital Board, Mr. Justice Stable suggested that there would be fewer actions for negligence against hospitals if patients were informed of what had happened.[1] "I have had reason," said his Lordship, "to deplore the number of actions which I feel are wholly ill-founded claims against surgeons and doctors for negligence. But neither the patient nor his relations really know what goes on inside the hospital. There cannot possibly be a bad mistake made which everyone in the hospital does not know about, and if the patient were informed it is likely that it would put a stop to the ill-founded claims. Otherwise the patient and his relations do not hear the facts until they are brought out in court."

Mrs. Lily Patten, a factory operative, was injured when a power press suddenly descended and caught her right hand. An orthopædic surgeon at a hospital advised that part of the middle finger should be amputated. The operation was carried out by a house-surgeon, who by mistake removed the top of the little finger. It appears also that an operation for the suture of a severed tendon in the injured finger was performed too late and all three middle fingers were bent in towards the palm. Nineteen months after the accident the whole of the middle finger was amputated.

Mrs. Patten sued her employers for negligence and breach of statutory duty in respect of the fencing of the press. She also sued the Birmingham Regional Hospital Board, the orthopædic surgeon, and the house-surgeon. The house-surgeon admitted liability and paid into court the sum of £500, but the board and the consultant denied liability. During the course of the hearing, however, the proceedings against the consultant were discontinued.

In evidence, Mrs. Patten said that the house-surgeon had told her that the first operation was a "terrible mistake." She had another operation after which she was told that an attempt had been made to save her middle finger. Since then she had been unable to unclench the injured hand and had had to pay a series of visits to the hospital physiotherapy department. She could not use her hand, and since the accident she had had dizzy turns, blackouts, and spells of trembling.

An independent surgeon said that an exploratory operation should have been carried out to ascertain whether a tendon was divided when Mrs. Patten first arrived at the hospital. The doctor on the spot was in the best position to decide what should be done, but the casualty officer, being a young man, should have sought a senior's advice.

Giving judgment, Mr. Justice Stable said that the hospital board "are liable with the surgeon who made the grave blunder, for substantially the whole of the present condition of Mrs. Patten's hand." He was surprised, and not a little shocked, that the board did not express great regret and accept full responsibility for the consequential damage. His Lordship awarded £2500 damages against the board, from which the £500 paid in by the house-surgeon would be deducted. Mrs. Patten also succeeded in her action against her employers, who were ordered to pay £459 1*s*. in damages.

This case perhaps lends point to the correspondence in which contributors have suggested a standard system for the identification of fingers.[2]

1. *Manchester Guardian*, Nov. 26, 29, 30, 1955; *Birmingham Post*, Nov. 26, 30, 1955.
2. Forbes, R. *Lancet*, Oct. 1, 1955, p. 721. French, A. *Ibid*, Oct. 8, 1955, p. 774. Loxton, G. E. *Ibid*. Sayle-Creer, W. *Ibid*, Oct. 15, 1955, p. 824.

# In England Now

*A Running Commentary by Peripatetic Correspondents*

OUR youngest burst into the bedroom last Sunday morning. "Quick, Daddy! Come and look. Father Christmas is here!" I groaned out of the second stage and murmured disbelief. It was no use, the casement was flung wide open and only a piercing arctic blast seemed to be holding a pair of small pyjama legs from complete extrusion. I was on the point of an explosive assertion that Father Christmas could do as he so-and-so liked about premature arrival at the big stores in October, but we preferred him to go to full term in this household. According to my reckoning he had a few days still to go. A crashing noise in the garden wrecked that line of argument, so I heaved out of a nice warm bed and peered into the dawn. I rubbed my eyes; standing on the lawn was a large antlered beast idly pulling down the rhododendrons. My mumbled soliloquy as to what in heaven or earth it might be was answered scornfully from the window "Reindeer, silly!"

At half past seven on a dark winter morning cerebration is not too brisk. There was considerable difficulty in correlating the Christmas myth with the reported location of the nearest herd of reindeer in Britain. They were several hundred miles away at Rothiemurchus when we last had news. The creature ambled across the shaft of light from the window. It was a red stag. Now red deer have a deplorable reputation as gardeners, so I pulled on some trousers and a pair of gumboots and rushed ululating into the dawn. Apart from tripping over the shrubbery, the manœuvre was a great success. The stag leaped over the wall and cantered away towards the farm. The victor of the campaign, red-faced and crowned with laurel, returned in triumph. But Senate and populace were ever fickle; imperium was left in the porch, weeping and wailing and gnashing of teeth within. I had driven Father Christmas away. It took the jingle of many pennies to recapture the magic of sleigh bells, and I doubt if I shall be completely forgiven until the stockings provide more convincing proof.

* * *

An experienced family doctor once claimed that he knew the seasons of the year by the prevalence of certain diseases. Instead of the "season of mists and mellow fruitfulness" he recognised a time of colds and frothy chestiness, and when others were declaiming

> "That the lowest boughs and the brushwood sheaf
> Round the elm-tree bole are in tiny leaf,"

he realised that once again the season of hay-fever would be upon him. So it is with the anxieties of the mothers who attend the child-welfare clinics. At present we are at the height of the mythology season. Should I tell my child that Father Christmas isn't real, or may I mislead him with just a little "white one"?

Alas, in these days, to maintain the myth a good deal of imagination and foresight rather than just a "little white one" are needed. No longer is it enough to dispatch a letter up the chimney in early December and then take no further action until an early hour on Christmas morning when the stockings are filled. There is the problem in the modern house of finding space in which to collect and hide the presents, the problem of the cynical, superior elder brother, and of course that well-known syndrome of insomnia santaclausia. At school the child meets a variety of related myths, all of which must be reconciled. In the world at large from early November Father Christmas seems to be ubiquitous. To explain his omnipresence, desperate parents have to invent spaceships far excelling the magic carpet of old, and if these fail to convince then relations and deputies of the real man are introduced. Meanwhile the shops seem to go all out to fool Dad as they invent Uncle Holly, Mr. Mistletoe, and others. Recently a sincere and earnest parent, before entering a store explained that Mr. Mistletoe who was in attendance inside, looked after Father Christmas's reindeer, but when the child tried to check this information he got nowhere. Now I am told that the child believes still in Father Christmas but not in Father.

* * *

The family seems to be accident-prone and there is always at least one member with at least one bandage. Third Child falls downstairs pretty often, but so far has only got a large bump on her forehead which responds well to chocolate and masterly inactivity. The other day she fell all the way downstairs at the same moment that Second Child fell off our 6-foot wall into the next garden. Neither was seriously damaged but Second Child then had two bandages, one on a septic leg from a previous abrasion, and one on an elbow after this unhappy landing off the wall. Next day he cut his toe at the paddling pool, so that was three dressings to do, more or less continuously, as one was always sandy or loose. Now we have a first-aid tin in a prominent place in the kitchen—labelled "Biscuits" I admit, but with a crooked red-paper cross stuck on the lid by First Child—containing most of the things one needs for this sort of caper. I'm thinking of including a tourniquet, as only last week Third Child, who is one and a half and full of folly, climbed on to the cold frame and attempted to walk up the midrib. Much bright red blood and broken glass, but only three cuts and no stitches needed. Great pieces of glass were protruding through her jersey under the arms, and neither frame nor jersey will ever recover.

As there are six grazeable knees at risk now, I never seem to put on a clean frock without getting blood on it; so I either go out bloodstained or with huge wet patches where removal with cold water has been ineffectually tried. But in 25 years we shall have more medical help in the family at times of crisis, for Third Child is obviously going to be a pathologist. She spent a long time eviscerating a stuffed black and white bear with great concentration, finally shelling out a mobile, walnut-sized tumour—his erstwhile squeak. This she bore away in triumph, leaving the body abandoned and spreadeagled on the mat, displaying that intense interest in the specimen and disregard for the patient's comfort that I associate with my husband's branch of medicine.

* * *

Dr. Quatermass III writes: "I fear many of your more gullible readers may have been misled by my well-intentioned but somewhat naïve terrestial colleague.[1] He is doubtless familiar with the theories of Galileo, and possibly those of Isaac Newton, but before offering advice to space-age students, I feel he should study Einstein's theory of relativity.

"The 84th precept of this exercise may be translated as: when mass approaches speed of light, mass approaches infinity; when mass approaches infinity time becomes zero.

"Einstein has not followed this to its logical conclusion, so it is left to me to point out that time having become zero, distance acquires a similar value. Thus a consultant leaving Earth for Sirius II to deal with a case, say, of antennitis sinister tertius superior (acute) would arrive at his destination while still attending his previous patient without any distance being recorded on his milometer. Any mileage claim for the vast distances you imply in your article will be countered by the regional board on the ground that the shortest distance between two points is through hyper-space, which takes less than no time and relatively little petrol."

* * *

"Milk?" said the astonished wine steward on the *Silver Javelin*, "Do you mean to drink?" "Yes," said I, looking at the minute apology for a ham sandwich which they had served, "to help this down." When he had recovered from his shock he explained that he couldn't possibly spare any of the stuff because he was only allowed 14 pints for the whole day. "Don't you ever get asked for milk?" I asked. "Oh no," he said, looking at me disapprovingly, "except very occasionally for very young children." It is time you grew up, my friend, he seemed to say. I had to content myself with a glass of milk stout, which I enjoyed as I always do; but on this occasion I did want milk.

As I drank my stout I pondered on the reason for this reluctance to serve milk as a drink on trains and often, too, in restaurants. It seldom, if ever, figures on the menus. When I ask for it I am met with a look of amazement and often, indeed, of mild horror. I feel as if I had been guilty of some misdemeanour. Is it effeminate to ask for milk? Is there some sinister Freudian implication in a fondness for this drink which so aptly accom-

1. *Lancet*, Nov. 26, 1955, p. 1135.

panies the noontide sandwich. American navvies and stevedores ask for it without a blush and receive it, already chilled in cartons, in the toughest of "joints." If one is lucky enough to find milk in an English restaurant it is usually served in a glass at room-temperature with a decided sense of personal obligement. "In case they are short for the teas, I didn't ask—I just took it out of the jug," is the sort of story one receives along with the milk.

A cheery-looking girl in a roll-top sweater tells us in the Underground and on the hoardings to drink more milk. I hope she will read this and be able to help me. I should so like to drink more milk, on trains and in lots of other places too. Could she discuss my request with British Railways and the Pullman Company? If she is successful, as I know she will be, will she see that milk is specifically mentioned on the menus like this: "Milk, chilled (½ pint), served in carton"? Then travellers will know that it can be asked for with impunity and it no longer will lurk in the non-listed class of contraband drinks.

* * *

A PÆDIATRIC BABY

I am a pædiatric baby. My life started rather early, 7 months or thereabouts, when I found myself breathing oxygen in my prem. unit to keep down my mortality-rate. It was there I first met the pædiatric man. He was so nice, and after a little while he introduced me to my mother and told me I was no longer a neonate and deserved a health visitor to help my G.P. (whatever that was). He said the M.O.H. had a nice one, so I thanked him kindly.

One day she came to see me and I was sick—eating the paint off my cot I expect—so she took me to the clinic where I saw a man who wasn't the pædiatric man but who said I should see the pædiatric man; so I went to see another man I hadn't seen before. He said I wasn't very sick but he supposed the health visitor and the other man were right and I'd better see the pædiatric man, so if I went home he'd fetch him to see how sick I was. Well, I must have been, for in no time at all I was in a glass box called a cubicle in a pædiatric ward in a pædiatric unit with a pædiatric nurse and a pædiatric registrar. I felt very important. Then joy of joys, in came the pædiatric man leading the pædiatric surgeon, and my head really began to swell.

It was all over in a trice and I was home again and sad, pining for my pædiatric man. My mother didn't understand and took me to the man who knew the pædiatric man, but he didn't understand either. The health visitor was worried and took me to the clinic man, and I hated him because he wasn't the pædiatric man. He murmured "maladjusted" and might have sent me to a special clinic man but my mother was frightened and took me home, and I pined some more. The man who didn't seem to be anybody in particular came to see me and promised to call the pædiatric man again, so I stopped pining and got better; but I was learning about things now, so I pretended not to be better and the pædiatric man was very nice and took me back into my glass box and told me stories about a place far, far away called London where there were lots of other pædiatric men but not very many pædiatric babies. I was happy again and felt very important and my head swelled some more. Lots of people came to see me and said how interesting I was; and they were shown how I worked and I realised I was more important than I'd thought, especially after I'd been screened by the pædiatric radiologist.

Then one day the most wonderful thing of all happened. The pædiatric man came in and whispered that he'd netted me a real American pædiatric man; and he had too, especially for me. I was terribly proud and my head swelled like anything, till they looked at me in a funny way and talked about special research which sounded the most important thing of all. Now would you believe it, next day five people called consultants came to see me about my swollen head and made the most exciting plans. If only I had been able to keep calm, if only I hadn't been so worked up about it all, perhaps everything would have been well; but my tummy began doing strange things, terrible things, the five wise men withdrew, and I was bundled up and carried away to a place called an isolation hospital where there were lots of other people, and there I forgot the pædiatric man till I was better.

I don't pine any more now. I'm a happy pædiatric baby and I just don't know what I'll do when I have to grow up. But I'm still only 3.

# Letters to the Editor

## THE FORGOTTEN PATIENT

SIR,—Having carefully studied Dr. Bickford's articles of Oct. 29 and Nov. 5 and the subsequent correspondence, it seems very desirable that you and your readers should be directly informed of the relatives' reaction. We believe that our views are representative of a fair cross-section of opinion of close relatives of mentally ill persons, since the 560 members of our association consist almost entirely of such people.

We have to say at once that in our judgment Dr. Bickford has, by exposing (in his latest articles and an earlier one [1]) the extremely serious shortcomings which undoubtedly exist in many of our mental hospitals, rendered invaluable service not only to the patients in question and their relatives but to the community as a whole.

It is incomprehensible to us that some of his professional colleagues should have challenged the fundamental accuracy of his description of mental-hospital conditions generally, for it must be within their knowledge that, whilst there are some "progressive" hospitals, these are far outnumbered by the "non-progressive" kind. The recent independent findings of the *Daily Express* investigator Mr. Merrick Winn cannot be dismissed so airily as Dr. Duncan (Nov. 12) would have us think.

We ourselves have for some time been gravely concerned by practically all the matters to which Dr. Bickford has referred and have by various means, including the submission of evidence to the Royal Commission and of memoranda to certain Members of Parliament and others, sought to bring these very things out into the light of day.

In our opinion, it is essential that not only relatives but the public generally should be made aware of "what goes on" in our mental hospitals—how else can we gain the public support which time and again we are told is a prerequisite to the remedial measures so urgently required? As to the need for public support, may we recall the final remarks of the Parliamentary Secretary to the Ministry of Health when replying on behalf of the Government in the debate of Feb. 19, 1954: "I am sure it [the motion] will make a great contribution to the support we must have from public opinion in the country in solving the problems of mental health"; and also the view of Dr. Edith Summerskill, stated in the House on May 4 last, "that whilst there are in mental hospitals these appalling conditions of overcrowding . . . there is no pressure group on behalf of mental patients." We observe the following comment in an article in the *New Statesman and Nation* of Nov. 26: "only as a result of a public outcry will the considerable sums needed for capital development be prised out of the Treasury." Furthermore, in your leading article of Oct. 15 you submit that more publicity is required for the work and needs of mental hospitals than of any other kind of hospital, and you conclude by claiming: "Illumination of the whole scene is necessary: first because the public is entitled to know what is, and is not, being done in its name, and secondly because conditions cannot be greatly improved until many more people accept a share of the responsibility and decide to help."

If then we accept that the Government cannot or will not move without more support or pressure from the public, is it not reasonable to suppose that regional boards and management committees, with their everlasting plea of financial restrictions, should be only too ready to publicise their problems in every possible way? Instead we find that Mr. Sargood (Nov. 26) and his fellow administrators have elected to draw a veil over the grim state of affairs which Dr. Bickford so forcefully and accurately described.[1] The reasons for this attitude are said to be that to do otherwise would (1) deter nursing recruitment, and (2) discourage the voluntary patient. However, we now note the following editorial opinion in the autumn number of *Mental Health*: "We believe that both dangers exist, but that nevertheless it is even more important that a true picture should be presented to the public, for in

1. Bickford, J. A. R. *Lancet*, 1954, i, 924.

this way alone will they become more educated and strong-minded and more ready to accept their own responsibility for the care of the sick—mental as well as physical." Some additional, though qualified, support of this view is contained in the *New Statesman and Nation* article of Nov. 26.

Mr. Sargood also says he knows that Dr. Bickford's statement "psychiatrists have failed to cure and discharge their patients" *could* cause concern and distress to the relatives. Is he really so naïve as to believe that relatives of the so-called "chronic" patients are so lacking in perception as not to be aware that at least in some hospitals such patients remain "medically uninteresting" and their relatives are accordingly *already* consumed with anxiety? The present policy of the hospital authorities of failing to make the facts widely known—if indeed not deliberately hiding them—represents, in our submission, a completely misguided outlook, for we are convinced that until this policy is reversed there is little prospect of enlisting public sympathy for the reforms which are so vitally necessary.

Dr. Bickford's articles are, of course, directed towards the stimulation of hope for the "chronic"—a motive which we should have thought to be deserving of the highest praise and utmost support of each and every one. We consider it lamentable that several of Dr. Bickford's colleagues do not apparently share this view.

If on no other count, Dr. Bickford's critics must concede that he is right in saying: "far too little thought is being given, surely, to the vast residual problem of the patients whose active treatment has been abandoned and who are medically forgotten." It is abundantly clear to us that this is a statement of sober fact. Bitter experience also dictates that we emphasise the truth of Dr. Bickford's reminder that once a person becomes a chronic patient "nobody will be interested in him." The plight of the "chronic" is, indeed, grievous in the extreme.

Where then can the relative turn for even a glimmer of hope? Only to the advancement of research, we believe; but here again Dr. Bickford has confirmed our own conclusion that the position in this respect is one of shocking neglect. Further substantiation of this is also provided by the *New Statesman* article, which alleges that "The neglect of psychiatric research by the Medical Research Council is scandalous and it has been left to a private charity . . . to sponsor projects for which public finance should certainly be provided."

Most assuredly the present conditions cannot be tolerated much longer, and we wholeheartedly endorse the four reasons which Dr. Bickford has stated in his convincing reply as having prompted him to write his articles.

W. CARTER
President.

Friends of Menston Hospital,
Leeds.

O. M. CRIPPS
Secretary.

## IN THE MENTAL HOSPITAL

SIR,—Some of those who have written under this heading show a very poor acquaintance with the history of mental hospitals. Dr. Houston, for instance, writes (Nov. 26):

"Many of our mental hospitals are a hundred years old and belong to the custodial period of psychiatry. If a schizophrenic entered a mental hospital it was intended that he should remain there for the rest of his life, locked up in a ward of 50–80 patients, in dull monotony relieved by an occasional walk round the prison-like concrete courtyard."

The use of the passive voice absolves Dr. Houston from the obligation to tell us in whose minds such an "intention" may be supposed to have existed. The "intention" is certainly not shown in any of the writings of the period; not only did the psychiatrists of the 1840s and 1850s intend to cure their patients, but they were confident that they could do it. Thus Arlidge in his well-known work on *The State of Lunacy* (1859):

"Were we at all singular in the assertion of the curability of insanity, we should endeavour to establish it by an appeal to the statistics of recoveries among recent cases in the different English asylums; but instead of advancing a novel opinion, we are only bearing witness to a well recognized fact substantiated by general experience."

Asylum recovery-rates collected by Thurnam (*Statistics of Insanity*, 1845) ranged from 33 to 60% of direct admissions. Going further back, the Hanwell Committee in 1839 proclaimed that their asylum was "strictly and literally a Hospital . . . as much a hospital as St. George's or St. Bartholomew's," and in 1837 Sir William Ellis of the same asylum was planning the aftercare of discharged patients.

Subsequent frustrations from many causes—official parsimony, inordinate growth of the asylums, retention of early cases in workhouses, defective numbers and quality of staff, disappointing results of promising lines of treatment, and others—form a complicated story from which many lessons can be learnt; but there is no evidence that the function of the mental hospital as a place of treatment was ever forgotten.

Cane Hill Hospital,
Coulsdon, Surrey.

ALEXANDER WALK.

## CHILDREN IN HOSPITAL

SIR,—The following experience may be of interest to your readers in connection with last week's article by Professor Illingworth and Dr. Holt.

Our three daughters have all had the tonsil and adenoid operation. A was 7 years old, B 5½ years old, and C 6 years old.

A was a confident, self-assured girl who accepted the necessity of the operation, and made the most of her stay in hospital. She did not enjoy it, but knew it had to be. We had no bad after-effects with her. We wrote every day so that she knew we were keeping contact with her, but I was not allowed to visit.

The second daughter, B, who went in at 5½, was a sensitive child. We built up the idea of the hospital beforehand, so she was looking forward to hearing that a bed was available. We told her it had come about half an hour before she was due in the hospital. She was very glad to go, packed her case, and took crayons and colouring books. She settled down happily, did not mind my leaving her, and was chatting to an older girl in the room with her.

Unfortunately the older girl had a temperature and had to be sent home, so our daughter was in a room quite by herself. Had I known this I should have asked to be allowed to see her, but no visiting was the rule. We wrote every day and sent little parcels. When I fetched her she hugged me, and said she was glad to have had some peace and quiet by herself. The sister said she had been a model patient. I think she was too frightened to be anything else and bottled it all up inside.

For weeks, even months, afterwards she woke every night several times screaming. I slept in the same room with her so that I might just speak quietly when she woke. She did not seem to hear me, and would look right past me and cry and cry. Very, very gradually it got better, but even at 9 years old she occasionally wakes crying with that strange far-away look we had for so long after her stay in hospital. I was not allowed to visit her.

The third daughter, C, was of rather the same sensitive temperament, not wanting to leave me, especially for a night, though we had given her that experience by staying with my mother for a few nights. We prepared her in the same way as B. She went off happily and settled down with the other children. I was allowed to see her for a quarter of an hour the day after the operation. I shall never forget it. She saw me in the corridor and held out her arms. I went to her and bent down. Her arm came round my neck and she pulled me down on to the pillow. "I've wanted you so much. I think they should have beds here for the mummies—it's dreadful without you." We stayed like that for a few minutes, quite content. Then she showed me her letters and cards, told me she had tried not to cry, but anyway had not cried so much as the big girl. Then it was time to go. She blinked very hard, but I was able to say: "I'm coming to see you tomorrow." I gave her a little parcel to open as soon as I had gone.

The next day I spent an hour and a half with her. We did all kinds of things—colouring, reading, and so on. My husband saw her that evening for a quarter of an hour, and the following day I brought her home. She could not get out quickly

enough. She had been very good—so very sensible for a small person.

The first night at home she woke a lot and did not want me to leave her once. We put her bed in our room so that I could be near and reassure her when she woke. She cried a lot the first week, but it grew less. After a fortnight she was ready to go back to her own room, and now sleeps quietly and soundly. But much less serious have been the effects on her, because I went to see her.

In addition to the matter of parents visiting, I would like to mention that in all these cases the anæsthetic was not given until the child had been taken into the operating-theatre. Just think of the young child's feelings on seeing the strange white-gowned figures—no familiar faces—and feeling very frightened and alone. Is it not possible to give the anæsthetic befo.e leaving the ward, so that the child goes to sleep in bed and wakes up with it all over?

A MOTHER.

## MANAGEMENT OF RESPIRATORY PARALYSIS

SIR,—Two accessories designed primarily to aid the management of respiratory paralysis have recently been made by Capt. G. T. Smith-Clarke, of Coventry.

*Foot-operated Suction Apparatus*

The obvious advantages of a foot-operated sucker are extreme portability, independence of a source of power (electricity, compressed gas, or water pressure), and cheapness. It should, therefore, be ideal for occasional or intermittent use in a hospital ward, a house, or an ambulance. The new sucker (fig. 1) was powerful and reliable when solely employed during a period of weeks for aspirating the air passages of a patient with respiratory paralysis and a tracheotomy.

It consists, principally, of a spring-return foot-pump of about 100 mm. diameter and about 750 c.cm. capacity, and a unidirectional valve mounted on the lid of a suction bottle. The bottle sits in a deep recess which gives protection, and the whole apparatus is robust though light (12 lb. 2 oz., weighed without pressure tubing). On testing it by pumping up a column of water the sucker easily produces a partial vacuum of a half atmosphere (about 15 in. Hg) and can in fact suck almost an atmosphere if the suction catheter is blocked. The surprising power of this pump is due to its comparatively large bore which is a special feature.

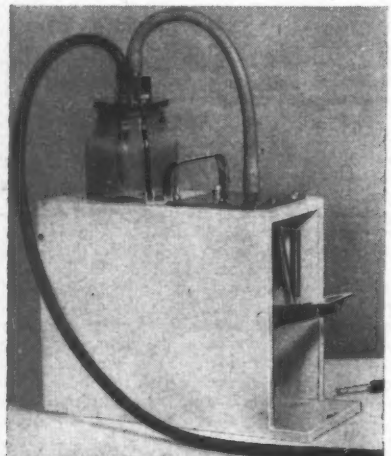


Fig. 1—Foot-operated suction apparatus.

As suction is only exerted on the down-stroke of the foot the effect is discontinuous. This lessens the possibility of the suction catheter producing an undesirable degree of partial vacuum in the bronchi. At the same time nothing is lost in efficiency since with each stroke the build-up of suction is virtually instantaneous. The degree of suction can be varied at will. If considerable resistance to suction suddenly develops, as it may if the eye of the catheter becomes jammed against the mucous membrane, it is immediately reflected in the resistance of the pedal, release of which abolishes suction and prevents drag on the tissues.

*Valve Assembly for Use with a Spirometer*

In the management of respiratory paralysis, frequent estimates of tidal air, minute volume, and vital capacity must supplement clinical assessment of respiratory insufficiency, to measure the ventilation achieved with a respirator or to follow progress in the recovery period.[1 2]

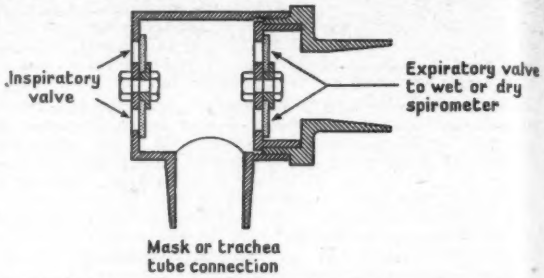



Fig. 2—Breathing-meter valve for measurement of vital capacity, maximum breathing capacity, or tidal air.

Such measurements can be made by leading the expired air to a dry or a water breathing meter and observing a series of breaths. In doing this it is inconvenient and inaccurate to have to displace, during inspiration, the face-mask or the connection to a cuffed endotracheal or tracheostomy tube. Though the difficulty is not present when an inspiratory/expiratory valve with a single expiratory vent is in operation, it is there at other times. The present device meets the problem by means of a pair of low-resistance inspiratory and expiratory valves arranged to allow inspiration only from air and expiration only into the spirometer (fig. 2).

We are indebted to Capt. G. T. Smith-Clarke, chairman, Group 20 Hospital Management Committee, Birmingham Regional Hospital Board, for much technical and other advice.

J. F. GALPINE
COLM BRADY.

Whitley Hospital, Coventry.

## CANCER OF THE FEMALE BREAST

SIR,—In his article (Nov. 26) Dr. McKenzie compares the 5-year-survival rates of patients of very different age-groups. But should not the difference between survival-rate of these age-groups in the population as a whole be taken into account? It seems to me that, for instance, the quotients of "normal" and patients' survival-rate would be a better basis for comparison; and assessment on this basis leads to conclusions other than those reached by Dr. McKenzie.

The Hague, Holland. F. P. HOLTZER.

## STAFFING LABORATORIES

SIR,—The consternation expressed by Mr. Snow and his colleagues (Dec. 10) is shared by others. The proposed new grading and salary-scales will increase the difficulty of staffing laboratories in the smaller specialised hospitals. To attain the higher category in the senior-technologist grade, the technologist of such a hospital will presumably have to transfer to a laboratory with a larger staff. Replacement will be virtually impossible. Even within the laboratory, the proposed scale may mean that a technologist of average ability, but with sufficient juniors working under him, will be paid more than a technologist of first-class ability in whose "division" the number of juniors is less. Such a system smacks of the Civil Service at its worst.

Remuneration in the higher grades of technology should depend on individual merit. Recommendation for the higher categories should be the prerogative of the pathologist-in-charge. An arbitrary formula, as in the new proposals, will lessen the responsibility of the pathologist and lead to discontent amongst his technical staff.

Women's and Maternity Hospitals, United Birmingham Hospitals. CLAUD W. TAYLOR.

1. Dall, C. W. Acute Phase of Poliomyelitis. Baltimore, 1954; p. 164.
2. Smith, A. C., Spalding, J. M. K., Russell, W. R. *Lancet*, 1954, i, 939.

## WHO ARE THE INFECTORS ?

SIR,—During 1953 there were 7913 deaths from respiratory tuberculosis in England and Wales, and 1751 of these occurred in persons who were not notified as cases of tuberculosis during life. In other words, apparently 1 in 5 of the persons who died from tuberculosis were not discovered in time to offer them proper treatment. With a falling mortality due to therapeutic advances, the *proportion* of cases dying unnotified has been rising since 1945, and it is surely among these unfortunate people that many of "the infectors" are to be found.

Let it be recognised that, although more tuberculous persons are surviving than ever before, this disease is still the outstanding killer of all the communicable diseases in this country and that more persons die of tuberculosis each year, than contract poliomyelitis. Our accepted standards of case-finding need critical re-examination.

Case-finding is the horse that pulls the cart of the whole tuberculosis programme, and Dr. Arblaster (Dec. 10) raises the interesting question whether the general practitioner refers enough patients for radiography. Usually this depends on the facilities at his disposal, because he often has to persuade his patient to be examined radiographically. It is a reasonable target for any chest clinic to seek to have at least 2% of the population it serves referred for radiography every year. In those clinics which have a camera unit or a general-practitioner X-ray service on the lines pioneered by Toussaint and Pritchard, this proportion of referrals is easily attained.

I share Dr. Barrow's scepticism (Dec. 10) about the known infectious tuberculous patient not being a risk to the community. This view has too long been accepted without challenge. Once the home and family contacts of such a case have been examined, how can one be confident that the patient is not in fact a source of casual infection to acquaintances who may be unaware of his condition ? The usual scheme of examining household contacts of tuberculous persons needs to be widely extended to include wherever possible close relatives living elsewhere, and other people in susceptible age-groups who are contacts at work or leisure pursuits.

One wonders, too, how many people are drawing National Assistance or a Service pension for tuberculosis without their condition being known to the medical officer of health. Is it not carrying professional secrecy to excess that these great organisations do not bring such cases formally to the notice of the M.O.H. ? It seems odd that, when every diagnosis of tuberculosis by mass radiography costs over £100, such inexpensive sources of case-finding remain untapped.

A further group of the community that merits scrutiny is the aged. It is probable that, as tuberculosis mortality falls, the infector pool will be driven into the older age-groups—especially older males. These people seem to be inaccessible to survey by mass radiography ; but how many patients in geriatric wards have had a chest radiograph since admission, and how many are tuberculin-negative—perhaps in close contact with a sputum-positive case of supposed "chronic bronchitis" ? Outside hospital the difficult task of persuading grandad with his old smoker's cough to have his chest examined falls on the general practitioner ; but it is no easy task to lead an elderly horse to water, let alone make him drink.

In your leading article (Nov. 26) you seem to accept an inevitable narrowing of the field that remains to be explored by mass miniature radiography. Now is this right ? Surely the situation is that M.M.R. is threatening to settle into a middle-aged routine when it is only a teen-ager in our medical armamentarium. For instance, is it really not possible for every unit to examine 80,000 persons annually instead of 50,000 ? Are units sufficiently mobile to tackle immediately small surveys and the epidemiological problems arising from newly discovered cases ? What can be done to enlarge the circle of M.M.R. examinees—at present too predominantly men and women who go out to work rather than old-age pensioners and housewives who stay at home ?

Dr. Parker (Oct. 29) has suggested that there is nothing magical about the epidemiology of tuberculosis, and that the practice of local authorities in respect of other notifiable disease can efficiently be applied to tuberculosis. I agree, but I suggest that if there were 7000 deaths per annum in this country from some of the communicable diseases that Dr. Parker mentions—for instance, smallpox—questions would be asked in Parliament, and many medical officers of health would have some sleepless nights. Our complacency in respect of tuberculosis is utterly amazing.

Bournemouth Chest Clinic. W. H. TATTERSALL.

SIR,—Your leading article does not mention the great strides that have already been made in finding some of the few highly infectious people who appear to be mainly responsible for the spread of tuberculosis.

Routine radiographic examination of special groups is invaluable, but the great help to general practitioners of "X-ray only" sessions must not be forgotten. Such sessions are a fruitful source of new cases of tuberculosis.

In this area it is believed that as a result of these daily sessions there has been a great drop in the infector pool. Thus during the last eighteen months 750 children under the age of 15 have been tuberculin-tested with the Heaf multiple-puncture instrument when attending the children's "X-ray only" sessions. The following are the numbers tested (which do not include any known contacts) and the percentage found to be tuberculin-positive :

| *Age (yr.)* | *No. tuberculin-tested* | *% positive* |
|---|---|---|
| 0–4 .. .. | 106 .. .. | 3·8 |
| 5–9 .. .. | 348 .. .. | 6·0 |
| 10–14 .. .. | 336 .. .. | 8·3 |
| Total .. | 790 .. .. | 6·7 |

In a previous communication [1] we gave some figures resulting from the examination of school-children in this area. In 1951, of 1903 children aged 11 to 14 tested with 0·1 mg. of tuberculin intracutaneously, 13·9% were found to be positive. This decrease in the proportion of tuberculin-sensitive children suggests that in the future we should have a drop in the incidence of new cases, but also that local outbreaks of disease will be more likely ; and we shall then be able to trace the source of infection in the same way as outbreaks of other infectious diseases are traced to their source.

Chest Clinic,
199, Station Road,
Harrow. R. GRENVILLE-MATHERS.

## CORONARY-ARTERY DISEASE

SIR,—In your leading article of Nov. 26, you rightly point out that the evidence for the thesis that coronary-artery disease arises from an excess of animal fat in the diet is far from complete, but I think you are in error in asserting that "we know of nothing that directly contradicts this hypothesis." I would refer to the virtual non-existence of coronary disease among the Eskimos and Lapps, whose diet in the long winter months consists largely of animal fat.

Seeking a more satisfactory explanation of the very striking war-time experiences of Norway, I think that the studies of Professor Keys and his colleagues, and the data of Dr. Bronte-Stewart, Professor Keys, and Professor Brock (Nov. 26), clearly point the way, especially if we bear in mind two facts emerging from these most important studies : (1) that in countries where the caloric content of the diet in general is low, the cholesterol content of the blood is also correspondingly low and coronary disease is rare ; and (2) that all those peoples with low cholesterol contents are known to be eaters of wholemeal or maize bread as their staple diet.

In the light of these two facts, it is my considered opinion that an all-important rôle in the decrease of circulatory diseases soon after the beginning of the German occupation of Norway was played by two factors : (1) the sharp decrease in the *total caloric content* of the diet (and not just of fats) ; and (2) the simultaneous compulsory change-over from white to wholemeal bread.

It is well known that white flour, which for the purpose of "improving" its colour and quality is subjected to agenising (i.e., treatment with nitrogen trichloride), becomes almost

1. Anderson, A. W., Grenville-Mathers, R. *Lancet*, 1952, ii, 330.

completely void of the natural vitamin E, which is present on the other hand in significant quantities in the chemically untreated wholemeal flour. Owing to the comparative lack of fat and protein foodstuffs during the war years, the daily consumption of this wholemeal bread in Norway rose considerably. How far-reaching is the importance of this second point is clearly demonstrated by the fact that the Bantu, whose staple diet is maize bread (with the highest vitamin-E content of all breads) is practically immune from ischæmic heart-disease.

It appears logical, therefore, to conclude: (1) that a high-caloric diet, coupled with low vitamin-E consumption, brings about, through the intermediary rôle of cholesterol, a high incidence of ischæmic heart-disease; and (2) that a low-caloric diet and large consumption of vitamin-E-containing food together give virtually complete protection against ischæmic heart-disease.

London, W.1. L. SCHMIDT.

## TECHNIQUE OF ADMINISTRATION

SIR,—I have read with considerable interest references in your columns to the technique of administration.[1]

I have had the pleasure of studying the principles and practice of management under Mr. R. G. Lathey and his staff during this past two years.

These principles have as their basis an organisation chart which should incorporate the actual and ideal relationships of organisation. This organisation chart should in addition be drawn up in functional units or under heads of responsibility. A 'Graphdex Manning Board' is probably the best medium for this chart.

The next step is to draw up written schedules of responsibilities for secondary and tertiary executives or professional heads and officers, and lists of duties for the junior members of the section concerned. These schedules should define the basic function of the person concerned, general and special responsibilities, limits of authority, and relationships with other members of the hospital staff. No reference is ever made to the manner in which the minutiæ of professional duties should be performed, other than to meet the requirements of the law (e.g., control of dangerous drugs).

These schedules are drawn up for all persons from junior technicians to myself, exclusive of course of the honorary medical staff. They are modified and improved upon the occasion of a new appointment.

It is by drawing up organisation charts and schedules of responsibility under heads of responsibility that one is able to see at a glance the span of control. I understand that the figure suggested by Mr. Graicunas [1] is an arbitary one, although a simple calculation will show the possible permutations and combinations of personal relationships that fall to the lot of a chief executive.

The organisation, or lack of it, of the nursing staff of the average hospital is such that the head of that service cannot satisfactorily resolve her responsibilities. A similar pattern is seen in the smaller technical departments, and is quite easily adjusted by a modification of responsibilities and an addition of executive levels within that department, with due regard for the number and duties of the staff concerned.

I do not believe that the general tone of Colonel Urwick's interpretation of administration [1] is applicable today. It smacks of a militant attitude—for example, authority is handed down from above. There is no need to require authority to be linked with responsibility since where one has earned it it is found to be unnecessary. Like Mary Follett I consider that authority comes from below as a result of doing one's job of working through others well, and that any decision made requires to be acceptable.

Any interpretation of discipline other than Sir Henry Taylor's would be useless if applied to many situations occurring in a hospital. The chief executive officer of a hospital is well advised to remember that he is associated with highly intelligent and skilled colleagues who are always willing to see other facets of a situation.

1. See *Lancet*, Oct. 8, 1955, p. 768.

Colonel Urwick maintains that investigation is the basic principle of management, and that the process of management (administration) is cyclic, utilising the other six principles—forecasting, planning, organising, coördinating, commanding (I prefer guiding), and controlling (i.e., in the sense of *knowing* that duties are in fact carried out in the proper manner).

Mr. Leslie Farrer-Brown, of the Nuffield Provincial Hospitals Trust, has written that facts do not themselves solve problems, but the fullest possible knowledge of them should help in the search for wise and effective solutions.

Invariably an acceptable solution to a difficult situation is found after a further examination of the facts.

I suggest, Sir, that more attention should be focused on the principles of management and the problems of human relations by those concerned with the training of hospital administrators.

It is far more important to widen one's horizon and learn to understand and work through others with special skills, than it is to be immersed in the detail of activity of each section of the hospital or to become a walking encyclopædia of procedure.

Royal Adelaide Hospital, Adelaide, South Australia. BERNARD NICHOLSON Medical superintendent.

## ATHEROMA

SIR,—Since first becoming acquainted with Duguid's work and theories on the pathogenesis of atheroma I have wondered at times whether this lesion can be found in those occasional patients who die of hæmophilia in middle age. The few pathologists I have asked have not been able to enlighten me. Dr. Levene (Dec. 10) raises this point again, for he suggests that fibrin deposition actually plays a part in the normal development of the aortic intima. It would be of interest therefore to examine carefully, and with the electron microscope if possible, the aorta of a hæmophiliac dying at any age.

May I inquire whether information is available on the appearances of the aorta and large arteries in hæmophilia. Presumably a patient with hæmophilia is immune from coronary thrombosis. Possibly he is immune from atheroma. But, instead, does his aorta develop abnormally?

London, W.1. H. WYKEHAM BALME.

## INSENSITIVITY TO VITAMIN D

SIR,—The report by Dr. Dent and his colleagues (Oct. 1) on the development of insensitivity to calciferol in postoperative tetany prompts me to record the following two cases of African women with this condition, thyroidectomy having been performed for simple nodular goitre.

The first patient, aged 25, was fully controlled on 1·25 mg. of 'A.T.10' daily until the cost of the drug prevented its further use. Therapy with calciferol was then instituted, and after three months control was established with a dose of 720,000 units (18 mg.) daily. Three months later, however, clinical and biochemical relapse occurred. This was corrected by the addition of 12 g. of calcium lactate daily to the above dosage of calciferol, since which time she has been well.

In the light of Dr. Dent's observations it is quite possible that in this case control is being maintained by calcium lactate alone.

The second patient, aged 21, has proved entirely refractory to therapy. There has been no response after 720,000 units (18 mg.) of calciferol for three months followed by 960,000 units (24 mg.) for one month, calcium lactate 6 g. daily being administered concurrently with the latter dose.

Thus this patient demonstrates that resistance to calciferol may occur from the outset.

Your annotation in the same issue mentions some of the implications of this phenomenon. In my own view its occurrence in the parathyroidectomised patient suggested a line of inquiry into the vexed problem of parathyroid/vitamin-D interrelations. The effect of sub-

liminal doses of 'Para-thor-mone' on the resistance to calciferol in the second patient is being investigated. However, it is clear that any effect which para-thor-mone may have in restoring sensitivity to calciferol will not explain Dr. Dent's observation of resistance to calciferol in patients with rickets and osteomalacia, in whom parathyroid function was presumably intact.

Baragwanath Hospital,
Johannesburg, South Africa. H. C. SEFTEL.

## NUTRITION AND VITAMIN $B_{12}$

SIR,—May I offer some comments on your leading article of Dec. 3, especially in regard to the administration of vitamin $B_{12}$ to children.

Our studies [1] in collaboration with Dr. Badenoch and Dr. Sinclair and other colleagues in different parts of the country have not been intended to investigate the general use of vitamin-$B_{12}$ supplements for children, and therefore could not be expected to provide the support for such use for which you are apparently searching. Suggestions [2] have previously been made in your columns that the lack of convincing evidence for the value of dietary supplements of this vitamin has been due to failure to study people who have been living for a considerable time on diets deficient in the vitamin. We have been fortunate in encountering such people amongst the vegan volunteers, and our primary object has been to characterise the signs of human dietary deficiency of vitamin $B_{12}$ sufficiently well to enable these signs to be utilised in studies on appropriate sections of the normal population, amongst whom children are of special interest.

In the group of about 150 vegans (*not* 32 as stated in your article) on whom we reported to the Second International Congress of Nutrition in Amsterdam in 1954, there were 33 children between the ages of 1 and 18, but detailed data were then available on only a few of these. However, the greater susceptibility of young children to vitamin-$B_{12}$ deficiency was recognised and attempts have since been made to extend our knowledge in this direction. Study of a considerable amount of further data on vegan infants and children leads us to believe that vitamin-$B_{12}$ requirements tend to become more critical after early weaning, when dietary supplementation with the vitamin may be more effective in children on diets very low in animal protein. Under such circumstances, the use of vitamin-$B_{12}$ dietary supplements would seem to be a wise precaution. The letters we have received from vegan parents whose children experienced vitamin-$B_{12}$ deficiency fully justify this warning.

Further information is greatly needed on the vitamin-$B_{12}$ content of different foods, especially those of vegetable origin. This might help to explain why so many of those living in the Middle and Far East manage successfully on diets quite low in animal protein. Is this due to their widespread use of fermented and germinated food? [3] The trace of vitamin B found in groundnut meal, for example, was probably due to moulds or bacteria which caused fermentation and at the same time produced the vitamin. During investigations [4] carried out in these laboratories several years ago on the effect of germination on the B vitamins in cereals and pulses, we prepared extracts of peas and soya beans in which germination was found to have produced slight traces of vitamin $B_{12}$—about 0·5 and 1·0 µg. respectively per kg. solids (W. F. Cuthbertson, personal communication). As germination had not been carried out under strictly aseptic conditions, the possibility could not be overlooked of this vitamin $B_{12}$ being produced by bacterial contamination. However, the production of traces of vitamin $B_{12}$ during germination of seeds has also been observed by Prof. W. H. Schopfer (personal communication), and these possibilities need to be considered in evaluating the vitamin-$B_{12}$ content of diets.

During attempts [5] to postulate theories explaining the physiological action of vitamin $B_{12}$, attention became focused on its cyanide content. We have advanced the hypothesis [6] that the cyanide may serve as a carrier of sulphur used for the formation of sulphur-containing metabolites which are essential in nutrition, and perhaps include methionine, which is known to be deficient in many vegetable proteins. This involves the formation of thiocyanate from cyanide, and has therefore led to studies [7] of thiocyanate metabolism in man. It would be of great interest to ascertain whether there is any relation between this thiocyanate metabolism and the sulphur deficiency recently implicated [8] in kwashiorkor, especially in view of the possibility now being explored [9] of its successful treatment with suitable mixtures of vegetable proteins together with vitamin-$B_{12}$ supplementation.

Ovaltine Research Laboratories,
King's Langley, Herts. FRANK WOKES.

## HEROIN

SIR,—One or two points in your editorial of Dec. 3 deserve comment.

Dealing with the question "Is heroin indispensable?" you say that the Standing Medical Advisory Committee's "No" was the only possible answer "in view of the facts (1) that the British Pharmacopœia Commission, with the authority of the General Medical Council, had in 1952 removed this drug from the pharmacopœia, and (2) that a great number of doctors, of all degrees of eminence, long ago dispensed with it in their practice."

So far as this second point goes, there must surely be many drugs which certain doctors never use in their practice; but is this a proper reason for banning their use by all doctors? Our answer to this question must surely be an unequivocal "No."

The decision of the British Pharmacopœia Commission in 1952 is worthy of further question. Is it not true that certain representations were made to them that if they removed heroin from the *British Pharmacopœia* it might then be possible for the Government to ban this drug? It would presumably be difficult or impossible for the Government to ban a drug which was included in the *B.P.* If, as I am suggesting, there was deliberate pressure on the British Pharmacopœia Commission to have heroin removed from the *B.P.* so as to facilitate later Government action, then that decision would appear to have been taken on political rather than medical grounds. Since heroin addiction is so rare in Britain, which manufactures and uses medically the largest amount, and so widespread in the United States which already bans it, one must surely ask what we hope to achieve by banning it here too. You partly answer this question by saying: "Whether much would in fact be gained by stopping all medical supplies has often been questioned, because anyone who has some morphine and a laboratory can turn it into heroin overnight."

It is flattering to the Fellowship for Freedom in Medicine that you should suggest that Her Majesty's Ministers have to choose between the Fellowship and the World Health Organisation. The Fellowship, however, is not alone in the belief that this ban is wrong in principle and cannot have the slightest effect on heroin addiction abroad. To its credit the *Times* has lent powerful support to this cause, and it surely cannot have escaped your notice that the British Medical Association also opposes this ban.

Your editorial, though true to the odd brand of intellectualism that erupts in your columns from time to time, is not a true reflection of the views of a sub-

1. Wokes, F., Badenoch, J., Sinclair, H. M. *Amer. J. clin. Nutr.* 1955, **3**, 375.
2. Pluk, C. V., Wokes, F. *Lancet*, 1952, ii, 1274. Wokes, F. *Ibid*, 1954, ii, 383.
3. Platt, B. S. Report of the 2nd Inter-African Conference on Nutrition, Gambia, 1952; p. 271.
4. Klatzkin, C., Norris, F. W., Wokes, F. *Int. Congr. Biochem.*, Cambridge, 1949.
5. Cooley, G., Ellis, B., Petrow, V., Beaven, G. H., Holiday, E. R., Johnson, E. A. *J. Pharm., Lond.* 1951, **3**, 271.
6. Wokes, F., Picard, C. W. *Amer. J. clin. Nutr.* 1955, **3**, 383.
7. Wokes, F., Picard, C. W. *Int. Congr. Biochem.*, Brussels, 1955.
8. Bigwood, E. J. *Voeding*, 1955, **16**, 143; Report of the 2nd Inter-African Conference on Nutrition, Gambia, 1952; p. 249.
9. Dean, R. F. A. Report of the 2nd Inter-African Conference on Nutrition, Gambia, 1952; p. 308.

stantial proportion of doctors in this country. Contrary to your concluding remarks, common sense no less than principle dictates that we, in Britain, should not ban heroin. Surely if any international gesture is needed we could agree not to export heroin. The addict will still secure his heroin whatever we do unless perhaps you, Sir, can persuade the United Nations to ban the growing of poppies.

Radlett, Herts. R. S. MURLEY.

## BLOOD-COAGULATION DEFECT ASSOCIATED WITH MISSED ABORTION

SIR,—Dr. O'Driscoll and Dr. Lavelle are to be congratulated on their interesting article published in your issue of Dec. 3.

I would like to say how much I agree with their advice that, once the diagnosis of missed abortion has been established, the pregnancy should be terminated without delay. If one waits for nature to expel the fœtus, as is so widely recommended, spontaneous evacuation may not occur for several months, during which time even the most placid woman is certain to be uneasy and anxious to have her pregnancy terminated. As Dr. O'Driscoll and Dr. Lavelle have, however, emphasised, a more urgent reason for termination is the likelihood of a blood-clotting deficiency developing if the pregnancy is allowed to continue. As regards their method of induction in cases of missed abortion after the 12th week, I would prefer the use of laminaria tents combined with an intravenous oxytocin drip. Tents are easier to insert than a stomach-tube, appear to be more effective in stimulating labour, and carry less risk of infection.

Dublin. DECLAN J. MEAGHER.

## ARTIFICIAL HYPOTHERMIA IN POLIOMYELITIS WITH HYPERPYREXIA

SIR,—We have read with great interest the article by Dr. Miörner and his colleagues (Sept. 17) and, to support their conclusions, we briefly report a similar case observed a year ago.

In November, 1954, a man of 32, of athletic build, was admitted with almost complete paralysis below the waist and beginning respiratory difficulties. The previous day he had had muscle pain in the limbs and the neck, but no other symptoms. The cerebrospinal fluid was characteristic of poliomyelitis. The paralysis rapidly ascended and after a few hours the patient had to be placed in a respirator. For two days the state remained unchanged, but on the third day he ran a high temperature, the heart-rate increased, and he became cyanosed and lost consciousness. His condition was not relieved by oxygen, strophanthin, plasma, fluid, and electrolytes. On the morning of the fourth day, in spite of all efforts, he became gradually worse, and signs of peripheral circulatory failure were apparent. His condition was considered hopeless.

This was the point at which artificial hibernation and hypothermia were started—Laborit's cocktail (chlorpromazine 1 part, promethazine 1 part, pethidine 2 parts) and cooling with ice packs, with the patient in the Drinker apparatus. His condition remained unchanged, his temperature was 31°C. From then on it gradually improved and at 28°C the circulation was satisfactory, and cyanosis disappeared. This temperature was reached in three hours, and it was at this level that the patient was then kept. On the slightest raising of the temperature circulation again became deranged. There was no shivering at any time. In the first three hours a dose of the mixture containing 2 mg. of chlorpromazine per kg. body-weight was needed, and subsequently about 0·1 mg. per kg. every half-hour was injected into the drip tube.

Ten hours after hibernation had been started the patient regained consciousness and even answered questions. Treatment was continued and his condition apparently remained unchanged, with regular cardiac rhythm and the patient as in a sleep. But after twenty-nine hours the heart suddenly stopped.

Post-mortem examination showed extensive bulbar and spinal involvement and destruction by hæmorrhages. The air passages were free.

We concluded from this case that the benefit of hypothermia in oxygen lack should be made use of in poliomyelitis when pyrexia and a failing circulation make it impossible to meet metabolic needs. The practice of withholding sedatives and hypnotics in poliomyelitis should certainly not be extended to the drugs used in artificial hibernation.

1st Department of Pædiatrics, Budapest University. P. V. VÉGHELYI.

Central Hospital of Infectious Diseases, Budapest. L. NAGY.

## KWASHIORKOR AND PROTEIN MALNUTRITION

SIR,—The cases of kwashiorkor described by Professor Brock and his colleagues (Aug. 20) are so similar to the cases of malnutrition seen in our hospital in Mexico City—not only in diet and age-distribution, but also in clinical lesions and biochemical findings—that we would like to make the following comments on their preliminary results.

1. The conclusions reached by Professor Brock and his colleagues are based on well-conducted trials that were aimed at finding the factor(s) responsible for the "initial cure" of the syndrome. The definition of kwashiorkor, by the F.A.O./W.H.O. Expert Committee on Nutrition in 1953, as a syndrome due to protein malnutrition—i.e., to relative deficiency of protein foodstuffs in the diet—does not emphasise sufficiently that the main protein foodstuffs are those which also contribute the largest portion of fat to the normal diet (for instance: meat, 6–40% of fat; milk, 3–4%; cheese, 10–40%; ham, 20–40%; eggs, 12%). Considering that a severe restriction of fats in the diet brings about, among other effects, a caloric deficiency that usually cannot be fully compensated by an excessive intake of carbohydrates,[1] children with kwashiorkor are deficient in calories; on the other hand, because protein foodstuffs are among the main "vehicles" of B vitamins, in the same way as fats are of fat-soluble vitamins, it seems more logical to speak, not of "protein malnutrition," but of "global malnutrition" or, simply, malnutrition. The diets reported by Brock et al. as consumed by their patients before admission to hospital "consist chiefly of maize (corn) porridge in Pretoria and Durban, whereas in Cape Town vegetables, such as squash . . . carrots, and potatoes are added to small amounts of cereal. The caloric intake in the Cape Town cases is probably less than in the Pretoria and Durban cases." The diet was inadequate in proteins, certainly did not meet the fat requirements, and was almost certainly deficient in several other nutrients.

2. The sequence of observed changes in the cases of kwashiorkor treated by Brock et al. is closely similar to those reported by Gómez et al.[2 3]—i.e., in the first 3–7 days the apathetic, irritable, and anorexic child becomes interested in its surroundings and may ask for food. Between the 7th and the 14th day after admission, the œdema disappears and the affected areas of skin desquamate. The serum-albumin reaches values of 2·5–3·5 g. per 100 ml. when the œdema has disappeared.

3. We agree with Brock et al. that the mortality-rate is variable, and that the first treatment consists, generally, in the emergency treatment of either the electrolyte disturbances or infection, or both. On the other hand, we have insisted [4] that the prognosis can be assessed fairly accurately if one considers the approximate weight deficit, and the presence or absence of electrolyte disturbances and infection. These factors influence the immediate outcome in contrast to the skin lesions of "kwashiorkor" or "pellagra" type, and the changes of the hair and mucosæ, and the œdema which have no bearing on the prognosis. In 733 cases studied by Gómez et al.[5] 46% of the deaths occurred in the first 48 hours after admission to hospital, and Brock et al. mention a mortality-rate of 70% during that same period. The over-all mortality-rate in Brock's cases was 20%;

1. Schwartz, R., Dean, R. F. A. *Brit. J. Nutr.* 1955, **9**, 230.
2. Gómez, F., Ramos Galván, R., Cravioto, J., Frenk, S. *Amer. J. Dis. Child.* 1954, **87**, 684.
3. Gómez, F., Ramos Galván, R., Cravioto, J. Frenk, S. Advances in Pediatrics. New York, 1955; vol. 7, p. 131.
4. Gómez, F., Ramos Galván, R., Cravioto, J., Frenk, S. *Acta pædiat., Stockh.* 1954, **100**, suppl. 43, p. 336.
5. Gómez, F., Ramon Galván, R., Cravioto, J., Frenk, S. *J. trop. Pediat.* (in the press).

and in the series studied by Gómez 23% in 1953, 21% in 1954, and 19% in 1955.

4. Our group for research on malnutrition reported in 1954 the results of treatment with and without the addition of extra vitamins in a series of 373 cases and controls.[3] The results reported by Brock et al. confirm that children with kwashiorkor (or malnutrition as we and others prefer to name this condition) do not need vitamins in addition to those present in the diet. The caloric consumption in our series fed on "free demand" amounted to about 35 per kg. body-weight per day during the first 5 days of treatment. Once the appetite improved, the children had an intake of 100–300 calories per kg. per day. These findings, similar to those of Brock et al. in Africa, are notable because the improvement is evident from the very beginning when the dietary intake is still far below the requirements of a normal child of the same body-weight.

5. The quantitative requirements of these patients are not the same in each phase of recovery. In the initial stage the child goes into positive nitrogen balance with very small amounts of protein (as has been previously demonstrated in protein-depleted dogs by Allison et al.[6]) and even in some clinical cases with proteins of low biological value, such as corn and beans.[7] As soon as the nutritional condition improves, and growth and development tend to reach a normal speed and pattern, the requirements are more selective and the needs of protein of high biological value increase.

Because we have been able to keep our cases in hospital for long periods, we have had the chance of observing and describing some of the clinical and biochemical changes peculiar to recovery.[8] These studies, and the knowledge that "initial cure" is not "actual cure," call for determination of the requirements of the different nutrients in the various stages of recovery. Only by such studies as that reported by Brock et al. can malnutrition be fully understood, and treatment placed on a scientific basis.

Group for Research on Infant Malnutrition, Hospital Infantil, México D. F., Mexico. RAFAEL RAMOS GALVÁN.

6. Allison, J. B., Anderson, J. A., Seeley, R. D. *Ann. N.Y. Acad. Sci.* 1946, **47**, 245.
7. Holt, L. E., Gómez, F. Unpublished data.
8. Gómez, F., Ramos Galván, R., Cravioto, J. *Pediatrics*, 1952, **10**, 513.

# Obituary

## ANTONIO EGAS MONIZ
### M.D.

THE name of Egas Moniz the neurologist was known all over the world: perhaps that was one reason why Egas Moniz the politician was less renowned outside Portugal. Yet few men have ever combined medical and political careers with such distinction. To medicine he gave cerebral angiography and prefrontal leucotomy, the adventurous moves of a bold mind, which won him a Nobel prize in 1949: to the councils of government in Lisbon, where he died on Dec. 13, he gave vigorous Liberal views which gained him the post of foreign minister and which, had not ill health hampered his later years, might have carried him to the presidency of Portugal.

[*Semaine des Hôpitaux, Paris*

To an already illustrious family, Antonio Caetano de Abreu Freire Egas Moniz was born on Nov. 29, 1874, in Avanca, a small village in the north of Portugal. As a young man, he went to the University of Coimbra, a picturesque little town whose affairs revolved around its university—a university of the best sort where a student's formal curriculum was not allowed to interfere too seriously with his enjoyment of the communal life of all the faculties. Literature, politics, philosophy, music, medicine: in this fruitful and competitive atmosphere, Egas Moniz was elected to the much-prized presidency of the Tuna Académica, the foremost of the student societies. He took his medical degree in 1899, and then stayed on for some years in Coimbra before his thoughts turned definitely to neurology and therefore to France, where many of the great neurologists were then teaching. In Paris he first met Babinski, Pierre Marie, Déjerine, and others with whom he long kept profitable contact. Of his contemporaries, perhaps Sicard, originator of myelography, was the man who had most influence on Moniz.

In 1911 a new chair of neurology was created in Lisbon. Egas Moniz was chosen to fill it, and he did so with honour for 34 years. His output of original scientific work from Lisbon began at once and continued at a great rate, with scarcely an interruption for the heavy political duties which he presently undertook with energy and ability.

He had entered politics much earlier—in 1900 when he was elected deputy for Estajerra. He was a left-wing monarchist, and his forthright views took him into the abortive 1908 revolution and into prison for a short time. But he came again, and he was appointed Portuguese minister in Madrid during a difficult period at the end of the 1914–18 war, when Portugal fought with the Allies, and Spain was neutral. In 1918, still professor of neurology, he became foreign minister and he led the first Portuguese delegation to the Paris peace conference. An event perhaps decisive then followed: a political quarrel led to a duel in 1919, and shortly afterwards he retired from politics. The political scene in Portugal may have seemed cramped to him and the medical one more satisfying; whatever his motives, after 1921 he gave his powers wholeheartedly to medicine and the Lisbon school, whose prestige he took to a high level.

In this new phase of his life, epidemic encephalitis was one of the first subjects that occupied his attention. And then, in July, 1927, he communicated to the Neurological Society of Paris the first news of cerebral angiography. In the years that followed he and his colleagues produced nearly 200 papers and monographs dealing almost exclusively with normal and abnormal cerebral circulation as studied by angiography. They first used sodium iodide as a contrast medium, but side-effects were troublesome, and it was some time before satisfactory results were possible with the use of 'Thorotrast,' a substance with which Dott in Edinburgh was also working at that time.

In 1935 Moniz attended the second International Neurological Congress in London, and heard Fulton and Jacobsen's paper on the effect of frontal leucotomy on the behaviour of the two chimpanzees, Becky and Lucy. After the operation, the animals lost the temper tantrums to which they had been prone when confronted with difficult problems. They remained alert, intelligent, and friendly, but it was no longer possible to induce an experimental neurosis. After the meeting, Moniz suggested to Fulton that a similar operation might help to relieve many of the unfortunate people in mental hospitals. Fulton and Jacobsen agreed, but they pointed out that bilateral removal of the frontal lobes would be a massive operation with a high mortality. But Moniz had other ideas, and returning to Lisbon, he set to work with a young neurosurgeon, Almeida Lima, who had lately returned to Portugal after training with Hugh Cairns at the London Hospital. In the first few operations they injected alcohol into the white matter of the frontal lobes, but later they used an instrument which they called a leucotome. This was a wire snare passed into the hinder part of each frontal lobe and then rotated to cut the white matter. The results at once aroused the widest interest and debate, and the subject was taken up in many parts of the world—notably by Freeman and Watts in the United States.

To put it at its lowest, the introduction of prefrontal leucotomy was the start of a profitable chapter in the study of the organic basis of mental disease; and indeed Moniz's work may be said to have persuaded many

people that there was in fact an organic basis worth studying. In the past twenty years more refined operations have produced better results; and though there have been disappointments, neurology and psychiatry still stand to gain yet more from the brilliant work of Egas Moniz.

## PATRICK ALFRED BUXTON

C.M.G., M.R.C.S., F.R.S., D.T.M. & H.

Professor Buxton, director of the department of entomology of the London School of Hygiene and Tropical Medicine, died on Dec. 13 at the age of 63.

His father, Alfred Fowell Buxton, was a former chairman of the London County Council, and his mother was the daughter of the Very Rev. T. W. Jex-Blake, a headmaster of Rugby and dean of Wells. Patrick Buxton was educated at Rugby and at Trinity College, Cambridge, where he held a fellowship from 1916 to 1921. He finished his medical training at St. George's Hospital, qualifying in 1917. After qualifying, he served abroad with the R.A.M.C. in Mesopotamia and North-West Persia. From 1921 to 1923, he was entomologist to the government of Palestine. During these years of travel he became interested in the wild life of the arid regions of the Middle East, and in 1923 he published his first book, *Animal Life in Deserts*. The next year brought him different experience and from 1924 to 1925 he studied the problem of mosquito-borne filariasis in Samoa and other Pacific islands. These *Researches in Polynesia and Melanesia* were later published as memoirs by the London School of Hygiene and Tropical Medicine.

[Stoneman

It was this postgraduate school of London University which, on his return to England, appointed him director of the department of entomology. He held this post until his death, first as reader and later as professor of medical entomology. He was one of the few remaining members of the original staff of the school, which came into being in 1927; and in the years in which he served it he contributed much to its present high reputation. He was elected F.R.S. in 1943 and appointed C.M.G. four years later. He was awarded the Mary Kingsley medal and in 1953 the Linnæan gold medal. He also served as a member of the Medical Research Council and the Colonial Medical Research Committee.

J. R. B. writes:

"As a scientific leader, Buxton applied just the right kinds of stimuli to research-workers in his department; and furthermore, by example and advice, he helped them to explain their results in good, clear English. Over many years, he fostered studies of the ecology of disease-carrying insects. Many investigations of this type, directly inspired by him, are summarised in his monograph on the *Louse* and in his final great work, the *Natural History of Tsetse Flies*. As his reputation became widely known, he was asked to visit many parts of the tropics to advise on problems of medical entomology, by such bodies as the Colonial Office, the Medical Research Council, and the World Health Organisation. Even in 1954, when not in the very best of health, he visited Singapore to preside over a conference on the threat of yellow fever, and later that year travelled about in Central America to study an epidemic of that disease. But, while his later time was much occupied by expert committees, he always took a full share of lecturing and other teaching duties at the school and he enjoyed getting to know his students. Scattered over the world, there must be many students of different races who will remember their warm welcome at his family home, when they were exiled alone in London.

"Some of us can remember occasions when Buxton was vigorously critical, for he never hesitated to point out indolence or inefficiency, especially in high places. But his colleagues and juniors will chiefly recall a paternal companion, widely travelled and extremely knowledgeable on all biological topics. Some of us, too, will recall a sympathetic and practical friend in times of difficulty or trouble."

Professor Buxton married Muryell Gladys, daughter of the late Rev. Hon. Talbot Rice, and she was associated with him in much of his work. She survives him with a son and four daughters.

## GEORGE RANKEN TUDHOPE

M.D., Ph.D. St. And., D.P.H., F.R.S.E.

Dr. G. R. Tudhope, lecturer in pathology at the University of St. Andrews, died suddenly on Dec. 12 at the age of 62.

A native of Newport-on-Tay, Dr. Tudhope received his professional education at the University of St. Andrews, graduating M.B. in 1918, and he devoted his whole life to the service of its School of Medicine. In 1922 he was promoted PH.D., and in 1937 the doctorate of medicine was conferred on him with honours and the award of a Rutherford gold medal for his thesis, which dealt with the distribution of reticulum as a means of differentiating sarcoma from diffuse carcinoma.

After holding house-appointments at Dundee Royal Infirmary he returned to the School of Medicine as assistant in the department of anatomy at what is now Queen's College, Dundee. His real interest, however, lay in pathology, and within two years from graduation he was appointed lecturer in that subject—a post which he occupied for thirty-five years.

W. J. T. writes:

"Dr. Tudhope's death deprives the university of one whose clarity of exposition made him an ideal teacher, while those who had the good fortune to know him mourn one whose personal qualities endeared him to all. A deeply religious man he was motivated, both in the performance of his professional duties and in the conduct of his life, by the highest principles—his watchwords being loyalty, integrity, and kindliness. The warmth of his nature was such that all who were in trouble turned to him instinctively for help and for solace; he will be sadly missed by his friends—he had no enemies.

"He dedicated his life to the service of others, to the best interests of the university, and to the care of the department for which he laboured so long and so loyally. Although he had many interests outside his profession, his contributions to the literature of pathology were many and varied, being a reflection of his width of knowledge and depth of culture. All his work in the field of research and as a teacher was notable for accuracy of observation and profundity of thought, while the attention he gave to his other interests was characterised by a constancy that was an inspiration to all who knew him.

"Of the many admirable traits in his character the most engaging was his cordial sympathy for youth; for him it was never a task but ever a privilege to undertake any duty on behalf of the student body. He will be long remembered, not only by medical students but by those of other faculties, for his appreciation of the dignity of man, for his patience with the wayward, and for his unfailing encouragement of the less able of his pupils. In a very special sense a debt of gratitude is due to him for the care he took both of the material and of the spiritual welfare of foreign students.

"In 1916 his fellow undergraduates elected him president of the Students' Union, and he laboured selflessly in its interests for over thirty years: in 1945 his son became in turn president of that body—a happy incident unique in its history.

"He was no less punctilious in the performance of tasks undertaken on behalf of his colleagues and professional brethren, as is witnessed by the fact that he was secretary of the Staff Club of Queen's College and member of the council of the Forfarshire Medical Association for twenty-nine years; he was president of the latter body in 1954–55.

"As warden of Airlie Hall, an all-faculty residence for men, he proved his sterling worth as a guide of youth; for his wardenship was marked by an atmosphere of happiness, an air of dignity, and a spirit of comradeship among those in residence which could develop only under the ægis of a really good man. In all his activities, but especially as warden, the courtesy and charm of his second wife was a fitting complement to his own many lovable qualities.

"He was chosen by his colleagues as their representative on the senate and court of the University, and his ability and fidelity were recognised by his election to the presidency of the Association of University Teachers of Great Britain."

Dr. Tudhope is survived by his second wife and his son (bearing the same christian names), who is lecturer in therapeutics at the University of Sheffield.

## WILLIAM BARR

**M.D., D.Sc. Glasg., D.P.H.**

Dr. William Barr, who retired from the post of medical officer of health and chief school medical officer for Rotherham in 1952, died on Dec. 2, at the age of 68.

In more ways than one he was an outstanding man. He came of Scottish farming stock; his parents farmed in Lanarkshire and they made many sacrifices to set him on the way to success. From the local grammar school he went to Glasgow University, where he graduated M.B. with first-class honours in 1908 at the age of 21. After eighteen months as an assistant in general practice among the colliery villages of Lanarkshire he was drawn to the public-health service, and in 1910 he took the B.SC. (public health) and the D.P.H. In those bygone days £250 a year was a wonderful salary for a first job, and in 1911 he obtained a post as school medical officer under Ayrshire County Council. In 1913 he became medical officer at the Glen Afton Sanatorium in the same county. Later in the same year he was appointed to the staff of Dr. J. R. Kaye, county medical officer of the West Riding of Yorkshire as assistant C.M.O.H. and tuberculosis officer in charge of the Rotherham Dispensary area of South Yorkshire. He was not released for service in the Forces during the 1914–18 war, and owing to overwork his health broke down. After the war he spent over a year, at first as patient and later as a medical officer, at King Edward VII Sanatorium, Midhurst. In 1920 he was appointed deputy medical officer of health and tuberculosis officer for Rotherham, and for the next five years he took an active part in organising the Oakwood Hall Sanatorium of 100 beds of which he became the first medical superintendent. A colleague remembers him at this time as

[Wrigley

"A tall thin, gangly young man, dressed in a single-breasted dark grey suit cut of unusual design, with a young keen face, wearing pince-nez and surmounted with the largest-brimmed felt hat that ever was. This was perched on the whitest head of hair—it was white even in those days. He was the sort of man who, if you met him for the first time in the street, you would turn round and have a second look at immediately you had passed him. In his features was the firmness of the poet; his head was that of the thinker; his dress that of the artist and individualist."

In 1925 he was appointed medical officer of health for the borough, and during the next twenty-seven years under his guidance the first steps in many useful public-health measures were taken at Rotherham. The Sheffield and Rotherham Smoke Abatement Committee, the first of its kind in the country, was formed at the borough's suggestion. Again Rotherham took the leading part in calling together the authorities which later formed the South-West Yorkshire joint board for the mentally defective. When the Midwives Act, 1936, came into operation and local authorities were empowered to employ midwives and to supply sterilised dressings for the mother's confinement, Rotherham had already for a decade provided maternity outfits and drums of sterilised dressings, and it had appointed an obstetric consultant for its maternity home and for district cases in 1929. In the same year it formed its voluntary tuberculosis care committee—nearly twenty years before such bodies were made compulsory by the National Health Service Act.

In dealing with school and preschool children, Dr. Barr always insisted that whatever service was started for one age-group should be provided for the other. A child to him was a child from birth to 15 years, and he recognised no artificial distinctions. This policy of coördination was carried further in 1938, when all the borough's health and hospital services were brought under the control of one committee with Dr. Barr as its adviser. When the hospitals were transferred to the regional hospital board in 1948 Dr. Barr did not lose interest in the hospital patients. He often said: "on admission they must have had a 'come from' and on discharge they must have a 'go to,'" and these were the concern of the local health authority. As a result of his attitude, Rotherham has always had a good working liaison with its hospital management committee.

His guiding personality had an effect outside Rotherham, for many of his assistants now hold senior posts in other towns. A few years ago he was appointed chairman of the standing conference of coöperating bodies dealing with atmospheric pollution under the Department of Scientific and Industrial Research. From 1949 to 1951 he was a member of the general council of the Queen's Institute of District Nursing.

F. C. C. writes:

"I first knew William Barr as a young man in 1913, and it has been a joy to have known him for over forty years. He was a thinker, a planner, and a man of infinite patience. He was also of high scholastic attainments. During his early career he had fought personal ill health and could never be said to be a robust man. No, he was a kindly man, and a wonderful observer possessed of a puckish sense of humour. He was a poet of no mean order. Verse flew from his pen faster than some of us could write prose. Another of his hobbies was conchology, and he had a large collection of shells. He lectured on this and other subjects of natural history to local societies. To William Barr all were God's creatures, and one feels proud to have known such a gentle and kindly man. He could see beauty in very ordinary things. Three years after he retired, he told me that these had been very happy years for him and that he was just as busy with his new interests as he had been with the old."

## Dr. C. R. ST. JOHNSTON

E. A. A. R. writes: "It was a privilege to be one of St. J's registrars in the post-war period, and to discover that factual knowledge was a mere skeleton without the historical associations and the social factors considered for each patient. His was an all-embracing outlook which reflected his own empathy with his younger colleagues' fortunes, and his sincerity and tolerance were at their best when one sought his help in the complicated clinical problem. His passing has left a void among those of us who knew him as a friend, a counsellor, and a fine Englishman."

S. C. D., writing of Dr. St. Johnston's work for the Walsall group of hospitals, recalls that he was appointed consulting physician to the Manor Hospital, Walsall, then under the municipality, immediately after his return to civilian life at the end of the war.

"On the nationalisation of the hospital service, St. Johnston became a member of the medical staff of the Walsall group, and assumed duties in addition at the General (Sister Dora) Hospital. From the inception of the new régime, he took a lively interest in its administration; he played an active part in drawing up the constitution of the medical staff bodies advisory to the hospital management committee, which anticipated by some years that since suggested by the Ministry of Health. His colleagues elected him to the first medical advisory committee, and he served on it continuously. At his death, he was acting as its chairman.

"He was as assiduous in his administrative as in his clinical duties; it was largely owing to his influence that the Sister Dora and the Manor Hospitals came to work in ever-increasing harmony, and the medical staff of the hospital group to regard themselves as a team, working in the interests of the group as a whole. To his high attainments as a physician many others will bear witness; my purpose is to pay tribute to the tact, patience, and judgment which made his services invaluable in committee both as a member and as chairman. He will be very deeply missed in the Walsall Hospital Group."

# Notes and News

## PUBLIC RELATIONS AND MEDICAL RESEARCH

DISCUSSING the dangers of over-stimulating public interest in disease, and of allowing people to expect too much, John M. Russell, in his report as executive director of the Markle Foundation,[1] New York, says that science must have better relations with its public if it wishes to avoid a repetition of the confusion and misunderstanding which arose over "the most publicized event in medical research during the past twelve months"—the use of the Salk vaccine for poliomyelitis.

Collecting money from the public for medical research came into its full bloom, he says, less than ten years ago. Tending more and more to suppose that, given the means, all scientific and health problems can be solved in almost no time, the public have been more than generous with personal contributions. The success of the money-raising campaigns of such organisations as the National Tuberculosis Association, the National Foundation for Infantile Paralysis, and the American Cancer Society has encouraged the formation of other similar agencies to form the spearhead of scientific attacks on other specific diseases, and today in the United States more than two dozen of them are collecting money and distributing it to educate the public and support research projects.

In these circumstances, Russell says, "educating the public" can have two meanings. "One is true education, where the facts of a situation are explained and advice given; the other is propaganda designed to attract the attention of the public, often by emotional means, and thus solicit support. Information that a disease can be prevented if detected early, and advice explaining where to go and what to do about it, is one type of education. The tearful posters and frightening statements sometimes made during money-raising campaigns is the other." For agencies dependent on personal gifts both types of "education" are essential; but a heavy responsibility now rests on the public-relations experts who are charged with raising the money. To have public-relations experts in science is a new development, and their potential influence—for good as well as for ill—is great.

In distributing funds for scientific purposes the Markle Foundation, and some other bodies of its kind, feel that they can be of most use by "encouraging our better young men to stay in academic medicine," and by supporting their research. Russell remarks that the methods used for distributing funds are important if the freedom of scientists is to be preserved and their integrity protected; for money can sometimes do harm, and money raised with too much enthusiasm and too little regard for the complexities of science carries a particular risk. The opinion of the public has become, in the U.S.A., an enormous factor in the support of research; but the public must be brought to understand that scientific research has its limitations and that basic scientific research takes a long time. Research, Russell rightly concludes, "is too essential to be abused or hampered just so money can be raised for its support."

## A PHILANTHROPIC RECORD

THE Ford Foundation is to give $500 million (£178 million) to colleges, medical schools, and hospitals in the United States during the next eighteen months.[2] This, the greatest single gift in the history of philanthropy, will far surpass the total amount disbursed by the Foundation since its establishment in 1936.

$210 million (£75 million) will be used to raise teachers' salaries in the 615 privately supported colleges in the United States, and is in addition to $50 million designated for this purpose last March.

The 3464 non-profit-making voluntary hospitals will receive $200 million (£71 million) to improve their facilities and service, to aid their staff financially, and for research. The amount allocated to individual hospitals will be determined by the turnover of patients and the number of births in the hospital. The American Hospital Association estimates that the voluntary hospitals contained 26% of the total number of beds in 1954, but received 61% of the admissions: 850,000 more beds are needed in American hospitals including 194,000 in general hospitals, according to the Public Health Service.

1. 1954–55 Annual Report of the John and Mary R. Markle Foundation, 511, Fifth Avenue, New York, 17, N.Y., U.S.A.
2. *New York Times*, Dec. 13, 1955.

Privately supported medical schools will get the remaining $90 million (£32 million). These schools, as well as public medical schools, now receive annual grants from the National Fund for Medical Education which was started in 1949.

## SHORTAGE OF HOSPITAL COOKS

SOME hospitals in the Midlands are threatened by paralysis in one of their vital organs—the kitchen. This threat of paralysis has been caused by an acute shortage of cooks, who can easily get higher-paid work in hotels and factory canteens in the area: the wage for a woman hospital cook is at present 123*s.* for a 48-hour week.[1]

One hospital management committee wrote recently to the Minister of Health asking him to consider raising the pay of hospital cooks or to authorise a special Midland rate. At one hospital, it says, the kitchen staff of three left in August, and since then the matron herself has done almost all the cooking for the hospital, working in the kitchen for seven days a week, sometimes for more than twelve hours a day, to the obvious detriment of her other duties. At another hospital, a porter has helped with cooking and serving breakfast; and a hospital official said that if the deficiency of cooks was not soon overcome the routine of many Birmingham hospitals would completely collapse.[2]

### University of Oxford

On Dec. 15 the degree of B.M. was conferred on the following:

J. V. Jones, D. R. K. Medley, J. G. Edwards, P. M. Higgins, Alexander Livingstone, P. C. E. Gould, Bryan Moore-Smith, R. M. Whittington, R. M. Ingram, W. G. Edwards, C. K. Davies, H. M. Hodkinson, A. G. MacIntyre, R. R. Sefi, A. D. Ferguson, M. J. A. Kelly, I. G. Thomson, J. G. Banwell, H. de la H. Davies, G. A. H. Miller, K. T. MacQuarrie, A. J. Smith, P. H. M. Carson, Michael Ashley-Miller, T. C. Wood, E. S. Robinson, A. H. W. Nias, F. S. Morgenstern, J. A. Tobin, Arnold Freedman, N. V. Morgan, Angela M. Howe, Margaret N. Williams, Ann Priestman, Barbara J. West, Anne F. Darquier de Pellepoix.

### University of Aberdeen

On Dec. 14 the following degrees were conferred:

*M.D.*—Muriel M. McLean (with commendation).

*M.B., Ch.B.*—I. V. Anderson, R. A. Bennet, Phyllis M. Cocker, L. D. Cruickshank, G. W. G. Hunter, M. S. Luckhoo, J. T. Sorley.

### Royal Faculty of Physicians and Surgeons of Glasgow

At a meeting of the faculty on Dec. 13, with Prof. Stanley Graham, the president, in the chair, the following were admitted fellows of faculty qua physician:

W. A. Dewar, T. S. Srinivasa Iyengar, Abdul Latif Minhas, J. R. Roy.

### Institute of Psychiatry, London

At the Maudsley Hospital, Denmark Hill, S.E.5, on Monday, Jan. 9, at 5.30 P.M., Dr. E. Stengel will give the first of five fortnightly lecture-demonstrations for postgraduates.

### Student Mental Nurses

The Nurses and Midwives Whitley Council have agreed to an increase of £15 in the basic training allowance of student nurses in mental hospitals and mental-deficiency institutions in the National Health Service.

1. *Times*, Nov. 30, 1955.
2. *Birmingham Evening Despatch*, Nov. 29, 1955.

Dr. Minna Gemmell has been appointed senior medical officer to the maternal and child-health nursing project of the World Health Organisation in Patna, Bihar, India.

# Appointments

BANKS, PHYLLIS B., M.B. Sheff., D.C.H.: school M.O., co. Durham.
COOK, MARGOT M., M.D. Basle, D.T.M. & H.: school M.O., Cornwall.
CORT, FRANK, M.B. Manc.: school M.O., co. Durham.
HARRIS, S. J., M.B. Lond.: appointed factory doctor, Nottingham West.
HOWELL-JONES, H., F.F.A.R.C.S., D.A.: consultant anæsthetist, Maida Vale Hospital, London.
JAMISON, H. M., M.B.E., M.C., M.B. Lond., F.R.C.S.: senior consultant general surgeon, S.W. Durham H.M.C.
MCDOWELL, C. R., M.B. Dubl., F.R.C.S.I.: asst. regional orthopædic surgeon, counties of Meath, Monaghan, Cavan, Louth, Longford, and Westmeath.
ROBERTSON, A. R., M.B. Glasg., D.P.H.: asst. county M.O.H., Derbyshire, and M.O.H., Bolsover.
WALKER, D. G., M.B. Sydney: registrar in general surgery, S. Devon and E. Cornwall Hospital, Plymouth.
WELSH, WALTER, L.R.C.P.E.: school M.O., co. Durham.
WRIGLEY, J. H., M.B. Edin., F.R.C.S.E.: consultant general surgeon, S.W. Durham H.M.C.

SOM

Ar
by s
hæm
by d
form
class
ary ;
is be
sonia
prim

Pe
inter
it ha
and
spina
cord
Af
still
this
Fort
of li
of th
In
gast
feel,

Ca
for c
Janu
weak
and
show
Bom
anæ
he w

Si

Ca
for c
he h
brea
the
inde

* Fr

Fig

# SOME SURGICAL ASPECTS OF ANÆMIA*

ALAN PERRY
M.S. Lond., F.R.C.S.
SURGEON TO THE LONDON HOSPITAL

ANÆMIA is commonly defined as a lack of blood shown by a reduction in the number of red cells or in the hæmoglobin content. It is usually caused by bleeding, by destruction of red cells, or by defective or deficient formation of red cells. When I was a student it was classified as primary—i.e., of unknown origin—or secondary; but with advances in knowledge the first category is becoming extinct, and even pernicious (Addisonian) anæmia can be no longer considered primary.

### Pernicious Anæmia

Pernicious anæmia has always had its surgical interest. With its achlorhydria and anorexia, it has often simulated carcinoma of the stomach, and the subacute combined degeneration of the spinal cord may resemble the effects of a spinal-cord tumour.

After the first world war splenectomy was still regarded as a possible form of treatment for this condition; but the results were bad. Fortunately in 1927 Minot discovered the value of liver as a remedy and surgeons were relieved of the need to oblige importunate physicians.

In cases where pernicious anæmia follows partial gastrectomy the operation is sometimes blamed. I feel, however, that this sequel is merely fortuitous.

**Case 1.**—In 1928 a man, aged 41, had a partial gastrectomy for chronic duodenal and gastric ulcers. He did well till January, 1954, when at the age of 67 he complained of weakness, wasting, and anorexia. His hæmoglobin was 56% and his colour-index 1·1. Radiography after an opaque meal showed normal post-gastrectomy appearances. Dr. R. R. Bomford regarded him as a straightforward case of pernicious anæmia and treated him with vitamin $B_{12}$. In August, 1954, he was perfectly well.

Similarly, a simple anæmia can follow a gastrectomy.

**Case 2.**—In 1947 a man, aged 46, had a partial gastrectomy for chronic duodenal ulcer. He did well but in June, 1951, he had to be readmitted with lassitude and shortness of breath. No bleeding was detected and no occult blood in the stools. Hæmoglobin 41%; red cells 3,800,000; colour-index 0·54. Opaque meal: no ulcer. A blood-transfusion (2 pints) was given and when seen in May, 1954, he had a hæmoglobin of 94%.

It should be borne in mind that patients with pernicious anæmia may develop carcinoma of the stomach. I will quote one case.

**Case 3.**—A woman of 63 was admitted on Dec. 30, 1946, under Sir Alun Rowlands, with Addisonian anæmia. Hæmoglobin 36%; red cells 1,630,000; colour-index 1·12 (fig. 1). Achlorhydria. She was treated with 'Anahæmin.' In November, 1951, the blood findings were: hæmoglobin 59%; red cells 4,400,000; colour-index 0·66. An opaque meal showed an enormous neoplasm at the cardia of the stomach (fig. 2), and on total gastrectomy on Nov. 23 a large cauliflower mass was found (tubular and papillary columnar-celled carcinoma) and secondaries in two lymph-glands. She died in the following April with stenosis of the anastomosis.

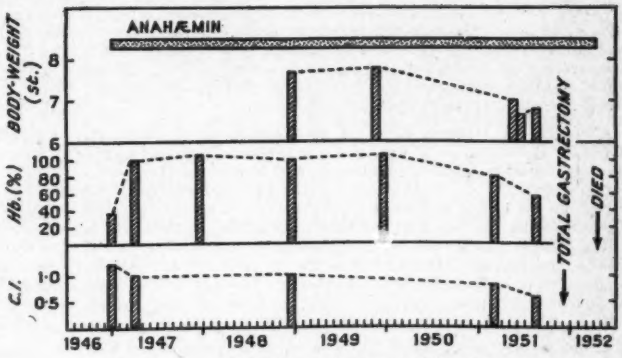



Fig. 1 (case 3)—Course of illness.

Of course it is possible for any patient with a long-continued anæmia to develop carcinoma of the stomach: in contrast to the cases which I shall describe later in which the carcinoma is the cause of the anæmia.

### Secondary Anæmia

*Acute* anæmia follows rapid loss of a large amount of blood—e.g., by trauma, massive gastric and duodenal hæmorrhage, or hæmorrhage from typhoid ulcer. The cause is usually obvious and treatment has been made relatively simple by the availability of blood-transfusion. More difficulty arises in cases where the losses of blood are small and often unnoticed, and the condition which first attracts attention is the anæmia.

*Chronic* anæmia occurs at all ages, and one must remember that it may be caused by carcinoma of the

* From the Schorstein lecture delivered at the London Hospital on Oct. 14, 1954.

Fig. 2 (case 3)—Neoplasm of cardia.

Fig. 3 (case 4)—Filling defect at incisura angularis.

Fig. 4 (case 5)—Filling defect in pyloric antrum.

stomach or of the large intestine. Its presenting symptoms—lassitude, shortness of breath, pallor, and so on—may mask the underlying lesion. It is my belief that such carcinomata do extremely well after appropriate surgical treatment, and I cannot emphasise too strongly the importance of full investigation, even to the point of exploratory laparotomy, in all cases of unexplained anæmia, whatever the patient's age.

### Carcinoma of the Stomach

With gastric carcinoma the digestive symptoms may be very slight.

**Case 4.**—A man, aged 70, came to outpatients in April, 1952, complaining of shortness of breath for four weeks. He had a good appetite and no indigestion; there was no obvious bleeding and he was fat. Blood: hæmoglobin 37%; red cells 4,200,000. Opaque meal: filling defect at the incisura angularis (fig. 3). On June 6, 1952, a high partial gastrectomy was performed, and a tubular columnar-celled carcinoma was found (no lymphatic glands seem to be involved). In August, 1954, he was very well, with normal blood.

**Case 5.**—A woman, aged 58, was admitted on June 28, 1954, for investigation of anæmia. In 1946 she had had treatment for duodenal ulcer and anæmia, and in 1953 an osteotomy for spondylitis. In September, 1953, her hæmoglobin was found to be 64%, and on a follow-up she was referred for investigation. When she was admitted in September, 1953, a lump was felt in the epigastrium, and an opaque meal showed a constant filling defect in the pyloric antrum (fig. 4). Hæmoglobin 81%. A high gastrectomy was performed, and a polypoid tubular columnar-celled carcinoma was found, with a secondary in one greater-curve lymph-gland.

**Case 6.**—A man, aged 65, was admitted in July, 1954, with a history that in 1940 he was in Mile End Hospital with epigastric pain, anæmia, and vomiting, and in 1952 with abdominal distension (opaque enema reported normal). He now felt tired but his appetite was good. Hæmoglobin 49%; colour-index 1·0. No mass was felt. He was fat, and there was occult blood in the stools. In hospital his hæmoglobin fell steadily; and though it rose to 83% when he was given 2 pints of blood, it was back in two weeks to 28%. On radiography no abnormality was seen: non-rotation not noticed. On Aug. 13 partial gastrectomy was performed for a hard plaque over the posterior wall of stomach, with division of bands for non-rotation. The pathological report was inflamed tubular columnar-celled carcinoma, with no growth in the three greater-curve lymph-glands examined.

The following case is particularly interesting because treatment seems to have been successful despite a long lapse of time between diagnosis and operation.

**Case 7.**—A woman, aged 70, had a hæmoglobin of 58% when examined on May 29, 1949, and an opaque meal showed a large filling defect; but she refused operation. On Feb. 18, 1950, her hæmoglobin was 38% (fig. 5), and a mass could now be felt, though radiography (fig. 6) showed little change; but she again refused operation. On Aug. 2, 1950, a high gastrectomy was performed, and the lesion was found to be a trabecular polygonal-celled medullary carcinoma, with no apparent spread to lymph-glands. In 1954 she was alive and well.

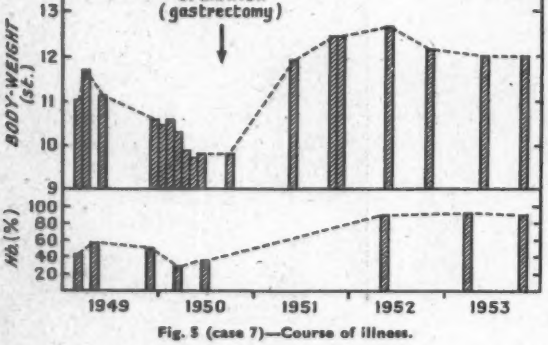



Fig. 5 (case 7)—Course of illness.

### Carcinoma of the Large Intestine

With carcinoma of the large intestine the patient may notice no bleeding, or he may have melæna, or the bleeding may be quite severe. Often the regularity of bowel action remains unchanged.

**Case 8.**—A woman, aged 50, was admitted on Aug. 19, 1951, complaining of the passage of some loose motions on holiday—possibly with some blood. Her hæmoglobin was 66%. On Sept. 2 sigmoidoscopy was normal to 25 cm.; hæmoglobin 70%. An opaque meal showed no abnormality of stomach, intestine, or colon. As all investigations had failed to explain the anæmia, laparotomy was undertaken on Sept. 19, and it revealed a carcinoma of the transverse colon near the splenic flexure. This proved to be a tubular papillary columnar-celled carcinoma, without involvement of glands. When the X-ray films were re-examined, no sign of any lesion could be found.

In the following case the picture was somewhat obscured by the patient being diabetic and alleging some menorrhagia.

**Case 9.**—A woman of 51 attended hospital on Feb. 10, 1950, complaining of flatulence. Her hæmoglobin was 69%, and a mass was doubtfully palpable in the right iliac fossa, but an opaque meal was negative. On Aug. 17, 1953, an opaque enema displayed an intracæcal mass (fig. 7), and on Aug. 26 hemicolectomy was performed for a mass near the tip of the cæcum, which was reported as tubular columnar-celled carcinoma partly mucoid. This mass measured 2 by 2 in., and I feel that in the clinical examination not enough stress was laid on the doubtful findings in the right iliac fossa. In 1954, however, the patient was still well.

**Case 10.**—A man, aged 62, was very pale when he first attended on Aug. 7, 1952. His hæmoglobin was 27%; an opaque meal showed prepyloric narrowing; and a test-meal 0·07% free hydrochloric acid. Later a mass was discovered in the right iliac fossa, and on Nov. 28, 1952, a right hemicolectomy was performed for what proved to be a tubular columnar-celled mucus-secreting carcinoma of the cæcum.

**Case 11.**—A woman, aged 59, was admitted on June 7, 1944, with anæmia. Her hæmoglobin was 59% and an opaque enema showed carcinoma of the transverse colon. On June 16 most of the transverse colon was excised, leaving a cæcostomy. Because of bombing she was evacuated to Scotland on July 6.

At a follow-up on June 1, 1953, she was pale and short of breath: hæmoglobin 45%. On Aug. 11, 1953, her hæmoglobin had fallen to 34%, and an opaque enema showed a filling defect near the hepatic flexure. At laparotomy a carcinoma was found about 3 in. from the site of the previous junction: partial colectomy was performed with end-to-end anastomosis. The pathological report was tubular columnar-celled carcinoma, with secondaries in one lymph-gland and fibrocaseous tuberculosis in nine.

### Congenital Conditions

A Meckel's diverticulum may contain ectopic gastric mucosa which ulcerates and bleeds freely enough to cause anæmia. Fortunately, as a rule in children the bleeding is severe and obvious and is dealt with as a surgical emergency, provided the child comes under a surgeon's care early enough.

Of many cases I shall quote three.

**Case 12.**—A girl of 8 months was admitted on Oct. 29, 1937, with increasing pallor and some alleged melæna. Her hæmoglobin was 19%, and her red-cell count 2,000,000. Despite blood-transfusions she went downhill, and she was referred to me by Dr. A. Maitland-Jones. We both thought ulceration in a Meckel's diverticulum the most likely cause of the hæmorrhage.

At laparotomy a small diverticulum was found in the left iliac fossa, adherent to the anterior abdominal wall. In view of the child's poor condition it was thought best to separate the bowel and embed the ulcer.

On Aug. 26, 1946, she was readmitted with intestinal obstruction. Laparotomy was performed and there appeared to be a large pouch lying in the mesentery of the small intestine—probably jejunum. This was excised with a portion of intestine. Examination showed that the pouch was lined

Fig. 6 (case 7)—Filling defect of pyloric end of stomach.

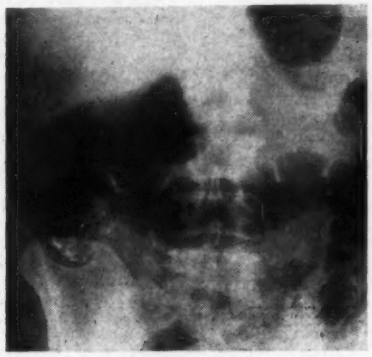


Fig. 7 (case 9)—Intracæcal mass revealed by barium enema.

Fig. 8 (case 13)—Distension of stomach with non-rotation.

by gastric mucosa, and there were two peptic ulcers—at the entrance and exit from the intestine, which was much narrowed.

This case illustrates the fact that ectopic mucosa can occur apart from a Meckel's diverticulum—though the original diagnosis was not very far out. It also illustrates the value of laparotomy where there is bleeding from the intestinal tract, even in the very young.

**Case 13.**—A boy born in 1913 was first seen in 1928, when he was said to have had severe bleeding from the rectum. His hæmoglobin was 21% and he developed papillœdema and retinal exudates with partial blindness of the left eye. In 1936 he was readmitted having had hæmoptysis five days previously. There was infiltration of the lower lobe of the right lung and his sputum contained tubercle bacilli. His left eye showed optic atrophy. He was sent to a sanatorium. In 1939 he was again readmitted, this time with rectal bleeding. His hæmoglobin was 78%. An opaque meal showed that a large portion of barium remained in the ileum. It was difficult to say whether this was in a Meckel's diverticulum, but it had not the appearance of being so. In April, 1940, the patient had some abdominal pain but no further bleeding. Laparotomy was performed and a Meckel's diverticulum excised. Its lining consisted of gastric mucosa, and there was a small progressive peptic erosion.

In 1951 the patient was well.

**Case 14.**—A woman, aged 44, first attended on Jan. 21, 1954, complaining of shortness of breath. Her hæmoglobin was 38%, and a test-meal showed no free hydrochloric acid. An opaque meal revealed nothing abnormal, but an opaque enema showed a dome-shaped filling defect in the cæcum. As there was a mass in the pelvis this defect was tentatively attributed to fibroids, but she had had no menorrhagia. At laparotomy on March 10, 1954, a Meckel's diverticulum was excised: it contained a small ulcer.

### Non-rotation of Intestine

During development the normal rotation of the cæcum and part of the colon to the right of the abdomen may fail to take place. Often adhesions form across the second part of the duodenum, causing dilatation of the duodenum and stomach. This may be associated with ulceration and hæmorrhage.

**Case 15.**—A girl, aged 11, admitted to another hospital in February, 1954, with an alleged hæmatemesis and a hæmoglobin of 28%, was treated by blood-transfusion. After her admission to the London Hospital on June 23, 1954, an opaque meal showed a markedly distended stomach and non-rotation (fig. 8): her hæmoglobin was now 83%. At laparotomy the condition of non-rotation was confirmed and the constricting bands were divided.

### Acholuric Jaundice

Acholuric jaundice might be described as a hereditary congenital anæmia due to imperfect formation of the red blood-cells. The spleen destroys large numbers of these poor products, causing hæmolytic jaundice and anæmia of lesser or greater severity. The destruction may occur in phases, producing attacks of more marked jaundice and anæmia. Splenectomy removes the destructive agent and converts a sick person into an almost normal one.

I well remember a young flying officer who had got into the Royal Air Force with this disease, and before the late war was invalided from Singapore as a case of pernicious anæmia. He was referred to me by Dr. Donald Hunter as a case of acholuric jaundice for splenectomy. His delight on the 12th day after operation that he could now wear green pyjamas had to be seen to be believed.

The following case is a classic.

**Case 16.**—Mrs. M. was born in 1884. In 1891, at the age of 7, she was admitted to Shadwell as a case of anæmia. In 1896 at the Brompton Hospital her spleen was found to be enlarged and her condition was diagnosed as splenic anæmia. When she was first admitted to the London Hospital, in 1902, this diagnosis was maintained, and in 1906 she was shown to the Royal Society of Medicine as a case of splenic anæmia. In 1908, on her readmission to the London Hospital, her red cells numbered 1,500,000 per c.mm. and her spleen extended to the right iliac fossa.

This was all, of course, before Chauffard discovered the so-called fragility of the abnormal red cells as measured against different concentrations of saline solution.

In 1923 she was readmitted with ulcerative stomatitis; hæmoglobin 55%; colour-index 0·71. Next, in February, 1932, she came in with a five weeks' history of abdominal colic, jaundice, and shivering. Her urine contained bile, and the fragility of the red cells was found to be increased. Plain radiographs of the abdomen showed shadows attributed to gallstones. On April 8, 1932, splenectomy and cholecystectomy were performed: the pathological report was: splenomegaly; acholuric jaundice; acute and chronic inflammation and fibrosis of gall-bladder.

In 1942 she was readmitted having had a swelling of the right breast for six months. Her hæmoglobin was 110%, and the red cells were hæmolysed at saline concentrations of 0·42–0·56%. A right radical mastectomy was performed, and the condition proved to be a tubular solid acinar scirrhous carcinoma, with secondaries in two out of seven axillary glands.

This patient's son also had acholuric jaundice.

**Case 17.**—He was 17 years old when in 1929 he was admitted having had jaundice for two months. (He had also had an attack three years before.) On examination he was deeply jaundiced, the spleen filled the left of the abdomen, and radiography showed shadows suggestive of gallstones. Hæmoglobin 75%; colour-index 0·77; fragility of red cells slightly increased (hæmolysis at concentrations up to 0·55% saline). In February, 1930, splenectomy was performed, but

not cholecystectomy; for though the gall-bladder was fatty, no stones were felt. A month later the red-cell fragility and other blood findings were unchanged. In 1932 he had acute appendicitis, and did well.

### Hæmangiomata of the Intestine

Intestinal hæmangioma is rare but can be important for the surgeon because the diagnosis cannot be definitely established without exploratory laparotomy. Unfortunately, very often, as in the case described below, the hæmangioma is too widespread for excision. Occasionally, however, it is more localised and can be treated effectively. I remember a case, with severe anæmia, in which blood could be seen spurting from hæmangioma, about an inch in diameter, in the wall of the rectum. This was destroyed by diathermy.

**Case 18.**—This patient was 35 years old when admitted on Dec. 28, 1951. His history was that in 1948 he had become increasingly tired and lethargic with headaches; his hæmoglobin was 33%, and for nine months he had liver injections with some improvement. On Dec. 11, 1951, his hæmoglobin was found to be 35%. Opaque meals showed no abnormality, but at operation on Feb. 8 we found numerous tortuous large vessels and vascular patches along the whole length of the small intestine (fig. 9). Unfortunately excision could not be attempted.

Fig. 9 (case 18)—Hæmangiomata of intestine.

### Splenic Anæmia

In the past splenic anæmia was often a dumping-ground, and cases were thrown to the surgeon in the hope that he might be able to elucidate some of the problems involved. The proportion of cases of anæmia given this diagnosis is nowadays diminishing; but they still have important surgical interest.

There are, I believe, three types in which operation can be of great benefit:

1. Cases of anæmia with enlarged spleen which in our present state of knowledge (or lack of it) must still be classified as splenic anæmia.

2. Cases of thrombosis of the splenic vein in which the enlarged spleen is an encumbrance.

3. Cases of portal hypertension—clinically corresponding to what is known as Banti's disease—in which vascular shunts are of value. Here portacaval anastomosis is now largely replacing the lienorenal anastomosis formerly undertaken.

I shall quote an example of each of these types.

**Case 19.**—This patient had attended medical outpatients for six years as a case of splenic anæmia. From time to time she was treated by blood-transfusion. The fragility of her blood-cells was normal, and her hæmoglobin varied between 43% and 67%. On Feb. 19, 1954, when her age was 34 and her hæmoglobin 43%, her spleen (which was six or seven times the normal size) was removed. No dilated veins were seen and the portal-vein pressure was 150 mm. water. The liver looked normal, but biopsy showed hæmosiderosis and fibrosis of the liver as well as hæmosiderosis of the spleen. Seen on June 21, 1954, she was perfectly well, with a hæmoglobin of 85%.

**Case 20.**—A boy, aged 9, who was attending the skin department for psoriasis, was found to have an enlarged spleen. When he was admitted on Aug. 29, 1949, his hæmoglobin was 81%. Someone had courage to do a drill biopsy of the spleen, and the result was negative. Tests of liver function gave normal results, and the Wassermann reaction was negative. After removal on Sept. 6, 1949, the spleen was found to weigh 1 lb. 10 oz. There was thrombosis of the splenic vein and the pressure in the portal vein was 265 mm. Unfortunately he developed a subphrenic abscess, but this was successfully drained. He has developed into a healthy normal boy who can now play all games.

**Case 21.**—This patient was 45 years old when she had the first lienorenal shunt performed at the London Hospital.

When admitted on Dec. 20, 1947, she had had swelling of the abdomen and hæmatemesis for sixteen months. Her abdomen had been tapped on several occasions, about 3 gallons being removed at the first time and about 1 gallon a week thereafter. Her hæmoglobin was 33%, but by blood-transfusions and a diet containing ample vitamins was raised to 83%. Liver-function tests showed some liver damage: plasma-proteins 6·2 g. per 100 ml. (albumin 2·9 g., globulin 3·3 g.).

The operation was done on Jan. 20, 1948, using an abdomino-thoracic incision. The splenic-vein pressure was found to be 380 mm. Splenectomy and left nephrectomy were undertaken, with end-to-end anastomosis of the splenic and renal veins over Blakemore and Lord 'Vitallium' tube. On Feb. 5 the peritoneal cavity was tapped and 3 pints of fluid removed.

She did very well till February, 1954, when at follow-through examination she was noticed to be pale. No obvious bleeding. On readmission on Feb. 16 her hæmoglobin was 30%. Her liver-function tests showed nearly normal figures. She was treated by blood-transfusion, and with iron and vitamin C. Seen on June 21, 1954, she was very well.

### Thrombocytopenic Purpura

Thrombocytopenic purpura is a very dangerous disease, far commoner in the female sex. It may occur at any age and is usually heralded by ecchymoses of the skin and mucous membranes. There is often profound constitutional disturbance; severe anæmia develops quickly; and as a rule the spleen is somewhat enlarged. The blood-platelets are greatly reduced in numbers, and the bleeding-time is usually lengthened; but the coagulation-time is normal. In these cases I have seen deaths from bleeding into the brain or into the myocardium.

The condition is comparatively rare in boys, and they tend to recover as they grow older. I have only once removed a boy's spleen for this condition; and my reason for doing so was largely his own desire to take part in the "brutal and licentious" games of our public schools.

So far as I know splenectomy is the only treatment; but the time of the operation has to be selected with the utmost care. During operation the injection of adrenaline into the splenic artery causes considerable shrinkage of the spleen, and it is said to squeeze out the platelets contained in that organ. The effect of splenectomy on the bleeding-time may be of three kinds:

1. Immediate and dramatic. On ligation of the pedicle the bleeding-time becomes normal, and it remains normal.

2. The bleeding-time may return at once to normal but then relapse for a time before returning again to normal.

3. There may be no immediate effect. Nevertheless the bleeding-time usually returns slowly to normal.

In most cases the platelet-count goes up fairly quickly—in a matter of a few days.

The results of splenectomy are on the whole excellent, except possibly in some of the older patients for whom the operation may have been delayed too long.

In conclusion I should like to thank all my colleagues on the staff of the London Hospital for their help and encouragement, and in particular Mr. J. E. Richardson and Mr. A. Anscombe for much assistance in the preparation of this lecture.

# DISTURBANCES OF CARBOHYDRATE METABOLISM CAUSED BY BARBITURATES AND ALCOHOL

RICHARD A. HUNTER
M.D. Lond., M.R.C.P., D.P.M.
LATE ASSISTANT TO THE DIRECTOR, YORK CLINIC, GUY'S HOSPITAL, LONDON

W. H. H. MERIVALE
M.B. Lond., M.R.C.P.
READER IN CLINICAL PATHOLOGY, GUY'S HOSPITAL MEDICAL SCHOOL

A. J. SMITH
M.B. Lond.
REGISTRAR, DEPARTMENT OF CLINICAL PATHOLOGY, GUY'S HOSPITAL

BARBITURATES and other sedative drugs are known to interfere with carbohydrate metabolism as reflected in the glucose-tolerance test. Tod (1935) found that the duration of hyperglycæmia was shortened by barbiturates, morphine, and chloral. Subsequent investigations showed that carbohydrate metabolism might be disturbed in several ways; but "lag" curves and prolonged hyperglycæmic responses predominated (Merivale and Hunter 1954, Hunter and Merivale 1954).

Hunter and Greenberg's (1954) report of 3 patients who were suspected of having islet-cell adenoma of the pancreas, but were subsequently found to be barbiturate addicts, shows the importance of these observations.

## Material

We have carried out pyruvate-metabolism tests, after oral ingestion of glucose, on 16 patients who had been receiving barbiturates either because of addiction or as treatment. The type of barbiturate, dosage, and duration of consumption are shown in table I; where information about dosage was unreliable, approximate figures are given. In view of the similarity between barbiturate and alcohol intoxication (Isbell and White 1953), we carried out similar studies on 7 alcoholic patients, details of whom appear in table II.

TABLE I—BARBITURATE CONSUMPTION IN 16 PATIENTS

| Patient no. | Sex | Age (yr.) | Type of barbiturate | Average daily consumption (gr.) | Duration of barbiturate consumption (months) | Reason for taking drug |
|---|---|---|---|---|---|---|
| B1 | M | 56 | Amylobarb. sod. | 6 | 2 | Medical advice |
| B2 | F | 35 | ,, | 12 | 3 | ,, |
| B3 | F | 34 | ,, | 6 | 3 | ,, |
| B4 | M | 46 | ,, | 6 | 12 | ,, |
| B5 | F | 52 | Pentobarb. sod. | 3 | 3 | ,, |
| B6 | F | 35 | Amylobarb. sod. | 6–12 | 2 | ,, |
| B7 | F | 38 | Phenobarb. | 3 | 108 | ,, |
| B8 | F | 34 | Amylobarb. sod. | 6 | ½ | ,, |
| B9 | F | 36 | Quinalbarb. sod. | 3–6 | 6 | ,, |
| B10 | F | 28 | Phenobarb. | 4 | 1 | ,, |
| B11 | M | 58 | Amylobarb. sod. | 6 | 24 | ,, |
| B12 | M | 38 | Pentobarb. sod. | 24 | 48 | Addiction |
| B13 | F | 25 | Quinalbarb. sod. | 6–9 | 8 | Medical advice |
| B14 | M | 42 | Amylobarb. sod. | 18–36 | 36 | Addiction |
| B15 | F | 47 | ,, | 12–18 | 60 | ,, |
| B16 | M | 52 | ,, | 9–15 | 24 | ,, |

## Method

The pyruvate-metabolism test, originally described by Williams et al. (1943) and modified by Joiner et al. (1950), was used.

Blood-pyruvate levels were estimated with the patient at complete bed rest. The patient was fasted, and blood taken without compressing the arm. The patient was then given 50 g. of glucose in 200 ml. of water and the same dose of glucose was repeated 30 minutes later. Blood was taken 60 and 90 minutes after the first dose of glucose, and the pyruvate levels estimated by the method of Friedemann and Haugen (1943). The normal range of these levels found by Joiner et al. (1950) is shown at the foot of table IV. We carried out this test on 5 healthy persons and the results agreed with those of Joiner et al.

TABLE II—DETAILS OF 7 ALCOHOLIC PATIENTS

| Patient no. | Sex | Age (yr.) | Approximate average daily alcohol consumption (oz.) | Duration of alcohol consumption (yr.) | Polyneuritis | Liver-function (bromsulphalein test) |
|---|---|---|---|---|---|---|
| A1 | M | 55 | >20 (whisky) | >10 | + | Normal |
| A2 | M | 59 | >20 (whisky) | >10 | + (delirium tremens) | Normal |
| A3 | F | 28 | 5 (whisky) | >2 | – | Normal |
| A4 | M | 45 | >15 (whisky) | >10 | + | Mild impairment, 10% of dye remaining at 45 min. |
| A5 | M | 40 | >20 (whisky) | >10 | + | Normal |
| A6 | F | 44 | ? | >1 | – | Normal |
| A7 | F | 33 | 4 (spirits) | 1 | – | Normal |

At the same time, capillary blood-sugar levels were estimated at 0, 30, 60, and 90 minutes by the method of Haslewood and Strookman (1939). The capillary blood-sugar levels were also estimated in 16 healthy persons. The results appear in table III and the accompanying figure.

TABLE III—CAPILLARY BLOOD-SUGAR LEVELS (MG. PER 100 ML.) IN 16 HEALTHY PERSONS WHO HAD RECEIVED GLUCOSE 50 G. AT 0 AND 30 MINUTES

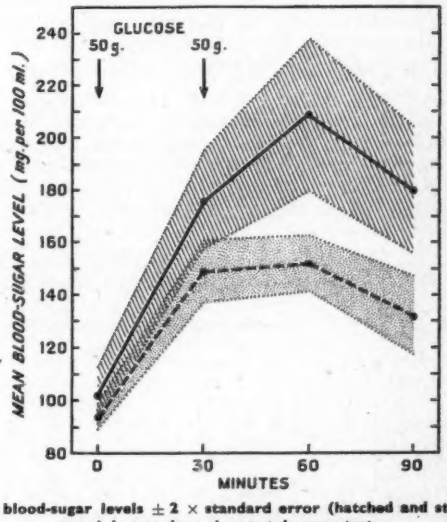
| — | Fasting | 30 min. | 60 min. | 90 min. |
|---|---|---|---|---|
| Mean .. .. | 93·8 | 148·6 | 151·8 | 131·7 |
| Range .. .. | 66–107 | 93–194 | 108–186 | 76–198 |
| Standard error .. | 2·4 | 6·1 | 5·2 | 7·5 |

## Results

### TWO-DOSE GLUCOSE-TOLERANCE TESTS

*Patients Taking Barbiturates*

The results are given in table IV. 2 patients (B3 and B6) responded normally to this test although their pyruvate metabolism was altered.




**Mean blood-sugar levels ± 2 × standard error (hatched and stippled areas) in two-dose glucose-tolerance test.**

Continuous line, 16 patients receiving barbiturates. Interrupted line, 16 healthy persons.

TABLE IV—BLOOD-SUGAR AND BLOOD-PYRUVATE LEVELS IN 16 PATIENTS RECEIVING BARBITURATES WHO HAD RECEIVED GLUCOSE 50 G. AT 0 AND 30 MINUTES

| Patient no. | Blood-sugar levels (mg. per 100 ml.) | | | | Blood-pyruvate levels (mg. per 100 g.) | | |
|---|---|---|---|---|---|---|---|
| | Fasting | 30 min. | 60 min. | 90 min. | Fasting | 60 min. | 90 min. |
| B1 | 70 | 140 | 168 | 140 | 1·14 | 1·29 | 1·27 |
| B2 | 156 | 156 | 196 | 169 | 0·70 | 1·81 | 1·04 |
| B3 | 95 | 154 | 151 | 128 | 0·95 | 1·76 | 1·67 |
| B4 | 101 | 134 | 162 | 154 | 0·60 | 1·21 | 1·71 |
| B5 | 100 | 157 | 182 | 171 | 1·26 | 1·03 | 1·06 |
| B6 | 77 | 177 | 146 | 109 | 0·85 | 1·10 | 1·70 |
| B7 | 108 | 158 | 205 | 191 | 1·18 | 0·89 | 1·39 |
| B8 | 96 | 125 | 176 | 155 | 0·57 | 0·82 | 0·91 |
| B9 | 63 | 275 | 268 | 257 | 1·60 | 1·40 | 0·50 |
| B10 | 111 | 177 | 166 | 161 | 1·98 | 2·28 | 2·35 |
| B11 | 110 | 187 | 225 | 162 | 1·06 | 1·57 | 1·84 |
| B12 | 91 | 205 | 247 | 216 | 0·98 | 1·45 | 1·34 |
| B13 | 96 | 203 | 380 | 307 | 0·57 | 0·83 | 1·60 |
| B14 | 104 | 195 | 211 | 170 | 0·96 | 1·83 | 1·18 |
| B15 | 123 | 203 | 230 | 193 | 0·78 | 2·07 | 2·22 |
| B16 | 127 | 169 | 219 | 191 | 0·74 | 1·55 | 1·94 |
| Normal range* | .. | .. | .. | .. | 0·40–1·12 | 0·58–1·26 | 0·54–1·34 |

* Joiner et al. 1950.

1 patient (B14), an incurable barbiturate addict, was studied on two admissions, separated by an interval of six months, with essentially similar results. Only the results of his first test are shown in table IV and included in the figure; both results are shown in table VI.

In the figure the means of the capillary blood-sugar levels are compared with those in the 16 healthy persons. The shaded areas represent the confidence limits, calculated as twice the standard errors of the mean values. The absence of overlapping of these areas at 60 and 90 minutes is strong presumptive evidence of a statistically significant difference between the two groups. It is not clear why the area for patients taking barbiturates is wider than that for the healthy persons.

*Patients Taking Alcohol*

These results are given in table V. All patients showed grossly abnormal responses in comparison with the "healthy" group. The interval between the two tests made on patients A1 and A2 was 2 days.

PYRUVATE-METABOLISM TEST

*Patients Taking Barbiturates*

The results are given in table IV. Only patient B8 gave a normal response to this test, but the result of the glucose-tolerance test was abnormal. She had been taking barbiturates for only twelve days before the test.

*Patients Taking Alcohol*

The results are given in table V. Patient A7 showed the only normal response to the test; she was the youngest of the group and had taken the smallest amount of alcohol. Patients A3 and A6 were tested three weeks after admission, during which time they had not had alcohol.

WITHDRAWAL SYNDROME AND VITAMIN B

Peters (1936) showed that thiamine acts as a co-enzyme or part of the co-enzyme system of pyruvic-acid oxidase. It therefore seemed to us that thiamine might correct the biochemical abnormalities we demonstrated.

We gave vitamin-B complex by intramuscular injection in the form of 'Becosym' (containing 10 mg. aneurine hydrochloride per ml.) 2 ml. daily for 14 days to 5 patients who continued to receive barbiturates. After this time the pyruvate metabolism test was repeated.

Results before and after the treatment appear in table VI. For comparison, 4 alcoholic patients received the same treatment but no alcohol; the results for this group are shown in table VII.

In both groups, the pyruvate levels largely returned to normal, or else the peak blood-level was decreased.

Patient B16, in whom the difference was smallest, was later found to have taken an extra large dose of barbiturate from a private source the day before the second test.

Although injections of vitamin B partly or completely restored pyruvate oxidation to normal, the results of the two-dose glucose-tolerance test were not so conclusive in the small number of patients who received the treatment.

## Discussion

Quastel and Wheatley (1932) showed that, in vitro, barbiturates interfere with the oxidation of pyruvates and glucose by brain tissue. Later, the same was found to be true of heart and liver preparations (Jowett and Quastel 1937). Himwich (1951) and his associates showed a decreased oxygen consumption in man during barbiturate anæsthesia.

TABLE V—BLOOD-SUGAR AND BLOOD-PYRUVATE LEVELS IN 7 ALCOHOLIC PATIENTS

| Patient no. | Blood-sugar levels (mg. per 100 ml.) | | | | Blood-pyruvate levels (mg. per 100 g.) | | |
|---|---|---|---|---|---|---|---|
| | Fasting | 30 min. | 60 min. | 90 min. | Fasting | 60 min. | 90 min. |
| A1 | 146 | 154 | 229 | 232 | 1·49 | 1·42 | 1·48 |
| A1 | 126 | 207 | 212 | 207 | 1·05 | 1·37 | 3·84 |
| A2 | 113 | 228 | 260 | 266 | 1·58 | 1·88 | 1·93 |
| A2 | 104 | 212 | 243 | 235 | 1·36 | 1·67 | 1·30 |
| A3 | 122 | 157 | 118 | 136 | 0·91 | 1·30 | 0·97 |
| A4 | 138 | 207 | 315 | 308 | 0·90 | 1·53 | 1·51 |
| A5 | 118 | 166 | 234 | 191 | 1·20 | 1·37 | 1·60 |
| A6 | 117 | 200 | 248 | 276 | 0·76 | 1·41 | 0·64 |
| A7 | 114 | 203 | 235 | 186 | 0·58 | 1·00 | 0·66 |

Our results show that barbiturates cause a widespread disturbance of tissue oxidation; this disturbance is not confined to nervous tissue, and it resembles that produced by alcohol. The resemblance between chronic barbiturate intoxication and chronic alcoholism, and the almost identical withdrawal syndromes, may therefore be caused by similar biochemical disturbances.

The effect of vitamin-B treatment on the pyruvate-metabolism and glucose-tolerance tests suggests that barbiturates retard carbohydrate metabolism by inhibit-

TABLE VI—BLOOD-SUGAR AND BLOOD-PYRUVATE LEVELS IN 5 PATIENTS RECEIVING BARBITURATES, BEFORE AND AFTER 14 DAYS' TREATMENT WITH VITAMIN B (BECOSYM 2 ML. DAILY BY INTRAMUSCULAR INJECTION)

| Patient no. | Blood-sugar levels (mg. per 100 ml.) | | | | | | | | | | | | Blood-pyruvate levels (mg. per 100 g.) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Fasting | | | 30 min. | | | 60 min. | | | 90 min. | | | Fasting | | | 60 min. | | | 90 min. | | |
| | Before | After | Difference | Before | After | Difference | Before | After | Difference | Before | After | Difference | Before | After | Difference | Before | After | Difference | Before | After | Difference |
| B12 | 91 | 106 | +15 | 205 | 194 | −11 | 247 | 280 | +33 | 216 | 231 | +15 | 0·98 | 0·59 | −0·39 | 1·45 | 1·06 | −0·29 | 1·34 | 0·99 | −0·35 |
| B13 | 96 | 106 | +10 | 203 | 182 | −21 | 380 | 266 | −144 | 307 | 193 | −114 | 0·57 | 0·58 | +0·01 | 0·83 | 1·02 | +0·19 | 1·60 | 1·17 | −0·43 |
| B14a | 104 | 96 | −8 | 151 | 182 | +31 | 203 | 165 | −38 | 119 | 156 | +37 | 0·83 | 0·72 | −0·11 | 1·64 | 0·89 | −0·75 | 1·22 | 0·94 | −0·28 |
| B14b | 115 | 132 | +17 | 141 | 138 | −3 | 188 | 192 | +4 | 127 | 180 | +53 | 1·57 | 1·04 | −0·53 | 1·75 | 1·40 | −0·35 | 2·26 | 1·25 | −1·01 |
| B15 | 123 | 106 | −17 | 203 | 173 | −30 | 230 | 166 | −64 | 193 | 154 | −39 | 0·78 | 1·07 | +0·29 | 2·07 | 1·41 | −0·66 | 2·22 | 1·43 | −0·79 |
| B16 | 127 | 109 | −18 | 169 | 147 | −22 | 219 | 165 | −54 | 191 | 157 | −34 | 0·74 | 1·10 | +0·36 | 1·55 | 1·66 | +0·11 | 1·94 | 1·21 | −0·73 |

TABLE VII—BLOOD-SUGAR AND BLOOD-PYRUVATE LEVELS IN 4 ALCOHOLIC PATIENTS BEFORE AND AFTER 14 DAYS' TREATMENT WITH VITAMIN B (BECOSYM 2 ML. DAILY BY INTRAMUSCULAR INJECTION)

| Patient no. | Blood-sugar levels (mg. per 100 ml.) | | | | | | | | | | | | Blood-pyruvate levels (mg. per 100 g.) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Fasting | | | 30 min. | | | 60 min. | | | 90 min. | | | Fasting | | | 60 min. | | | 90 min. | | |
| | Before | After | Difference | Before | After | Difference | Before | After | Difference | Before | After | Difference | Before | After | Difference | Before | After | Difference | Before | After | Difference |
| A1 | 126 | 100 | −26 | 207 | 129 | −78 | 212 | 169 | −43 | 207 | 203 | −4 | 1·05 | 0·74 | −0·31 | 1·37 | 1·00 | −0·37 | 3·84 | 1·10 | −2·74 |
| A2 | 104 | 94 | −10 | 212 | 184 | −28 | 243 | 181 | −62 | 235 | 180 | −55 | 1·36 | 0·68 | −0·68 | 1·67 | 1·04 | −0·63 | 1·30 | 1·04 | −0·26 |
| A4 | 138 | 82 | −56 | 207 | 154 | −53 | 315 | 187 | −128 | 308 | 179 | −129 | 0·90 | 0·49 | −0·41 | 1·53 | 1·06 | −0·47 | 1·51 | 1·30 | −0·21 |
| A5 | 118 | 79 | −39 | 166 | 148 | −18 | 234 | 182 | −152 | 191 | 159 | −32 | 1·20 | 0·42 | −0·78 | 1·37 | 1·00 | −0·37 | 1·60 | 0·98 | −0·62 |

ing pyruvate oxidation, and by other ways as yet undetermined. For example, barbiturates may influence the rate of absorption of carbohydrate from the gut.

*Withdrawal Effects*

When barbiturates were withdrawn from patients whose carbohydrate metabolism had been restored to normal or near normal by injections of vitamin B, withdrawal symptoms were mild and short-lived, and the patients suffered only slight distress. 2 of them had previously had epileptic fits and confusional psychoses after sudden withdrawal of barbiturates. Vitamin-B injections may similarly modify the withdrawal symptoms in chronic alcoholism.

*Electro-encephalography*

Since the normal electrical activity of the brain depends on the oxidative metabolism of glucose and possibly of pyruvate, interference with carbohydrate metabolism may account for the electro-encephalographic abnormalities produced by barbiturates.

Shimazono et al. (1953) showed that in man the characteristic fast waves caused by the intravenous injection of amylobarbitone sodium could not be elicited during hypoglycæmic coma. Clearly, such interference cannot take place when the brain is deprived of glucose, its natural fuel, as in hypoglycæmia (Peters and Van Slyke 1946).

Electro-encephalograms were taken of the 5 patients treated with vitamin B while receiving barbiturates. 4 patients were improved after two weeks of vitamin-B treatment; the alpha rhythm became more stable, and there was lessening of the fast and slow activity characteristic of barbiturate intoxication.

*Conclusion*

If our observations are confirmed, in assessing the value of vitamin B in psychiatric disorders account will have to be taken of whether the patients have been receiving barbiturates. Otherwise any improvement may be erroneously attributed to vitamin B, and vitamin-B deficiency may be wrongly diagnosed. The improvement may, in fact, be the result of withdrawing the barbiturate. Barbiturates may cause deterioration in mental illness (Hunter and Greenberg 1954, Hunter 1955). Our results may provide a biochemical explanation for this observation.

### Summary

Disturbances of carbohydrate metabolism, shown by the two-dose glucose-tolerance and the pyruvate-metabolism tests were found in 16 patients taking barbiturates. Similar disturbances were found in 7 alcoholic patients.

There is evidence that such disturbances account for the electro-encephalographic abnormalities produced by barbiturates.

These abnormalities may be corrected by administering vitamin B, even if the patient continues to take barbiturates. Vitamin B considerably modifies the withdrawal symptoms in barbiturate intoxication.

We thank Mr. M. P. Curwen, of St. Bartholomew's Hospital, for statistical advice; and the physicians of Guy's Hospital and Dr. L. C. Cook, of Bexley Hospital, for access to patients under their care.

### REFERENCES

Friedemann, T. E., Haugen, G. E. (1943) *J. biol. Chem.* **147**, 415.
Haslewood, G. A. D., Strookman, T. A. (1939) *Biochem. J.* **33**, 920.
Himwich, H. E. (1951) Brain metabolism and cerebral disorders. Baltimore.
Hunter, R. A. (1955) Barbiturate addiction. Paper read at British Pharmacological Society meeting, Bristol.
— Greenberg, H. P. (1954) *Lancet*, ii, 58.
— Merivale, W. H. H. (1954) *Guy's Hosp. Rep.* **103**, 375.
Isbell, H., White, W. M. (1953) *Amer. J. Med.* **14**, 558.
Joiner, C. L., McArdle, B., Thompson, R. H. S. (1950) *Brain*, **73**, 431.
Jowett, M., Quastel, J. H. (1937) *Biochem. J.* **31**, 565.
Merivale, W. H. H., Hunter, R. A. (1954) *Lancet*, ii, 939.
Peters, J. P., Van Slyke, D. D. (1946) Quantitative clinical chemistry. Baltimore; vol. II.
Peters, R. A. (1936) *Lancet*, i, 1161.
Quastel, J. H., Wheatley, A. H. M. (1932) *Proc. roy. Soc.* B, **112**, 60.
Shimazono, Y., Okuma, T., Fukuda, T., Hirai, T., Yamamasu, E. (1953) *Electroenceph. clin. Neurophysiol.* **5**, 525.
Tod, H. (1935) *Biochem. J.* **29**, 914.
Williams, R. D., Mason, H. L., Power, M. H., Wilder, R. M. (1943) *Arch. intern. Med.* **71**, 38.

## CERVICAL VERTIGO

G. M. S. RYAN
M.B. Lpool, M.R.C.P
CONSULTANT PHYSICIAN, ST. HELENS GROUP OF HOSPITALS
S. COPE
M.D. Leeds, M.R.C.P.
SENIOR MEDICAL REGISTRAR, ROYAL SOUTHERN HOSPITAL, LIVERPOOL

IN many cases of vertigo the cause is obscure (Symonds 1952). We are convinced that the neck plays a larger part in the mechanism of vertigo than is generally thought, and we have demonstrated its significance in vertigo of various types.

### Vertigo due to Cervical Spondylosis

We have seen several cases which we believe fall into this group, but most have had some complicating factor which might make the cause suspect, and we describe one case only.

**Case 1.**—A man, aged 57, had been in excellent health "since a baby." While he was building a wall a brick had struck him on the head; his neck was flexed at the time and the blow jarred his neck to one side. He felt "sick and dizzy" for a few moments but was not unconscious, nor did he fall. On recovery from the shock he noted a severe pain across the back of the neck and up the back of the head, made worse by bending the neck backwards, and particularly on looking to the left. He carried on with his work throughout the day, and, apart from the pain, felt quite well. On lying down that night he had a sudden and fairly severe attack of vertigo—"everything started going round and I felt sick." He did not vomit, and after a minute or two the vertigo subsided; but the neck pain did not allow him much sleep. For the following two days the pain remained severe, but it slowly subsided and was gone entirely within two weeks. During this time he noticed that on lying down or on looking upwards with the neck extended, he experienced intense, brief bouts of vertigo. These also gradually became less severe, and by the time the pain had disappeared they were troublesome only on bending the head far back. Throughout this time he had

no other symptoms. He was free from headache and had no dizziness other than that described; there were no aural symptoms, and none suggesting compression of nerve-roots or the spinal cord.

*On examination* the patient was well built and well nourished. His blood-pressure was 170/100 mm. Hg, and there was slight atherosclerosis of a degree commonly found in his age-group. There were no abnormalities in the central nervous or other systems. He was referred to the Liverpool Ear, Nose, and Throat Infirmary, where a detailed investigation was negative. On bending the patient's head backwards and to the left, he immediately had pain, identical with that which he had experienced since his accident. He was then placed flat on a couch, and his head and trunk lowered over the end in the manner described by Gordon (1954). At once he complained of vertigo, and we noticed that nystagmus appeared in association with this symptom. The vertigo and nystagmus occurred irrespective of whether the head was to the left, central, or to the right, and disappeared if the patient maintained his position for a little time. His head and neck were then held rigidly in relation to each other, and the manœuvre was repeated with the patient on his back, and on his left and right sides, care being taken to ensure that he was tilted with his head as far back as before. He did not have vertigo, nor was there any nystagmus. These procedures were repeated several times at intervals, on each occasion the same results were obtained.

*Radiography* of the cervical spine showed osteo-arthritic changes with slight lipping of c3–7 and slight disc narrowing between c4 and c7. The osteo-arthritis, with narrowed spacing and marginal sclerosis in the posterior joints extended as high as c2–3.

The minor trauma which this man suffered was highly unlikely to have caused intracranial damage, nor did he have headache or any other symptom suggesting such damage. He insisted that his neck was the seat of his pain, and at a later stage of his illness the pain was reproduced only by certain movements. Vertigo was related to movements which caused the pain and could be induced only by such movements of the head on the neck. The injury was relatively trivial, and we suggest that it alone would not have caused the lesion. We believe that the injury merely acted as a trigger mechanism, the fundamental cause being the underlying cervical spondylosis.

### Post-tractional Vertigo

**Case 2.**—A man, aged 60, was involved in an explosion in 1942 and he subsequently complained of pain and paræsthesiæ in the arms. Radiography showed cervical spondylosis, with prolapse of the discs between c3 and 4 and c5 and 6. He was sorely troubled by his symptoms, and for some years was given various forms of physiotherapy with only temporary relief. In April, 1953, he was subjected to manipulation, and thereafter slow neck traction was applied for three minutes daily for four days. The following day traction was applied, rather more strongly, for eight minutes; but this was not immediately followed by any symptoms. Three days later on getting up in the morning he had an acute attack of vertigo and fell to the left. There was no vomiting, sweating, or syncope. On trying to move to the right or the left he experienced vertigo and was unable to walk straight. He stayed in bed for a week and then got up cautiously, finding that the vertigo was brought on only by rapid movement of his head. The symptoms slowly diminished and had disappeared within two weeks. At no time was there pain, diplopia, or syncope. He had no history of ear trouble, and general and aural examinations were negative. Since then there has been no recurrence of the vertigo, but the symptoms attributable to the disc lesion have again become troublesome.

**Case 3.**—A married woman, aged 46, had had a hysterectomy five years previously, but apart from this had been in good general health. When first seen in August, 1953, she said that five years ago she had noticed a prominence of the left side of her neck, and a little later stiffness of the neck had developed which began to affect her in attacks lasting for a few days to a few weeks. During the previous year the discomfort in the neck had been accompanied by a pain in the right arm, and for the past three weeks before she had had similar pain in the left arm. There was no history of neck injury or ear trouble, and she had no other symptoms.

*On examination* flexion, extension, and lateral flexion of the neck caused pain in the back of the neck, and there was a doubtful area of partial anæsthesia down the outer side of the left forearm, and on the inner side of the right forearm. The remainder of the central nervous system was normal, as were the cardiovascular and other systems. The blood-pressure was 135/65 mm. Hg, and there was no detectable atherosclerosis. Radiography of the cervical spine showed considerable "lipping" of c4 and c5, and a rudimentary cervical rib on the right side. A cervical-disc lesion was diagnosed and the patient was referred to an orthopædic surgeon for treatment.

*Treatment and progress.*—On Aug. 27 the cervical spine was manipulated, and daily neck traction, together with active and passive movements was started. On Sept. 7, a day following rather more vigorous treatment than usual, she had a severe attack of vertigo; and these attacks continued, a violent one occurring while the physiotherapist was massaging her neck. Consequently all treatment was stopped. After about two weeks her vertigo was much less, but she still had torticollis and limitation of all neck movements. On Oct. 14, since the vertigo had gone completely, gentle massage was again attempted; but, after four days of this treatment she once more began to have vertigo and a spasmodic neck pain radiating up to the vertex and downwards. These symptoms subsided in about two weeks, and there was now no pain or paræsthesiæ in the arms. Subsequently very gentle neck traction was applied with no recurrence of the vertigo. By Nov. 8 the patient was very well; her neck movements were much more free, and there was only slight spasm. This satisfactory state of affairs was maintained, and she was discharged after a further month.

In these two cases, as in the first, there was considerable spondylosis of the cervical spines which predisposed them to further injury. There was a clear relationship between the neck traction and the vertigo, stretching acting as the trigger mechanism. In these cases the neck must have been directly injured, and this confirms our belief that the site of origin of the vertigo was the cervical region.

### Post-traumatic Vertigo

**Case 4.**—A married woman, aged 45, who had been well throughout her life, fell on to the base of her spine and also injured the back of her head. She did not lose consciousness, and her main symptom was severe pain at the bottom of her back; she also had slight pain in the occipital region. About three weeks after this injury she was wakened in the night by a throbbing sensation in the right side of her neck; and in the morning she sat up in bed, felt her head swimming, and fell to the left. This sensation, which was momentary, was accompanied by slight nausea. About ten minutes later she "felt fine," and got up to do her housework. Just before luncheon she looked up at the warming-rack and then bent down to attend to the stove, and immediately the kitchen "seemed to spin round" to the left, and she fell on to her left side. Simultaneously she felt "as if something went in her neck on the top part of the right side," and she had an "agonising pain" accompanied by nausea, but no vomiting. She thinks that she was unconscious for a minute or two. Within five minutes she was able to sit on a chair; the vertigo had ceased but a vague soreness persisted in the neck. Her doctor ordered her to bed where she had stayed for some six days before being seen at hospital. While in bed she found that bending the neck produced attacks, but that these were definitely subsiding.

*General examination* and aural investigation were negative. Radiography of her cervical spine showed no disease.

*Treatment and progress.*—A plaster cast was made to hold the patient's head and neck firmly in relation to each other. Tipping the patient, as previously described, did not produce vertigo while the cast was worn. The cast was then removed and the patient tipped with her neck bending freely; there was an immediate bout of vertigo, accompanied by nystagmus. These manœuvres were repeated several times, on each occasion with identical results. Within two months all her symptoms had disappeared and it was no longer possible to induce the vertigo.

**Case 5.**—A married woman, aged 40, slipped and fell on to the back of her head in June, 1954. She was unconscious for a few seconds and was carried to the welfare centre, where she stayed for over an hour because of shock and vomiting. She was unable to return to work because of

"feeling sick," and she also had some pain from abrasions on the left arm and left buttock; but was able to travel by bus that evening to attend her doctor's surgery. The next day she had a severe pain in the occipital region. This persisted but after five days she returned to work. In the second week of August the pain had spread to her left arm, and she was sent to hospital for radiography, which, she was told, "showed damage to the upper part of the spine." About this time she noticed that she was holding her head to the right side, and that her neck was stiff. She was advised to wear a collar, which she did for six weeks with considerable relief of symptoms. Some time later she had a severe attack of vertigo, with a feeling that her environment was rotating in a clockwise direction. Since then the attacks had occurred twice a week, and on two occasions she had fallen to the ground and bruised herself. When seen by one of us in January, 1955, the patient complained of occipital headaches lasting a few minutes and relieved by analgesics, attacks of vertigo, and stiffness of the neck which was painful on attempting to turn it to the left.

*On examination* the patient looked healthy, and no tenderness or other abnormality was detected in the occipital region of the skull, but there was considerable tenderness over the upper cervical spine. Movements of this region of the spine were painful, and were greatly limited, particularly rotation to the left and extension. She tended to hold her neck slightly flexed to the right. There was no evidence of injury to the brain, spinal cord, or peripheral nerves; but although she was left-handed, the grip in this hand was slightly weaker than in the right hand. The other systems were normal.

*Radiography* of the cervical spine was reported on as follows: 'there is evidence of a fracture of the spinous process of the fourth cervical vertebra with downward displacement of the distal fragment. There is no evidence of bony union. No other bony injury is shown. A cervical rib is present on the right side with a 'buttress' type of transverse process of the seventh cervical vertebra on the left side."

It is interesting that case 4, like case 1, insisted that the neck was the seat of the trouble. In case 5 the story is again one of trouble with the neck, vertigo developing after a latent interval, longer than in the other cases. Physical signs were confined to the upper part of the neck, and radiographic examination confirmed that the cervical spine was the site of the disturbance.

## Discussion

*Cervical Spondylosis*

Vertigo is rare; Sir Russell Brain (1954) did not mention it in his Heberden oration on cervical spondylosis, nor was it mentioned in a discussion of rupture of the intervertebral disc at the cervical level (*Proceedings of the Royal Society of Medicine* 1948). Cervical spondylosis was not included by Denny Brown (1949) in a review of the neurological aspects of vertigo.

Barré (1926) first referred to the possibility of vertigo occurring in cervical arthritis, and it is described as one of the many features of the Barré-Lieou syndrome. Mayoux et al. (1951) considered this syndrome by no means uncommon, and they claimed to have seen eleven cases in one year.

Headache and facial pain as a result of "cervical discopathy" was described by Neuwirth (1952), who remarked that vertigo may be a part of the clinical picture.

Wildhagen (1951) selected ten cases of Ménière's disease which he attributed to cervical arthritis, claiming that the latter brought about permanent labyrinthine upset. We cannot agree with this; but in four of his patients all tests of auditory function were normal, and we think it possible that these cases fall into our group.

Finally, a passing comment by Dix and Hallpike (1952) in their work on "positional nystagmus" due to otolith disease is of great interest:

"In a good many subjects pain in the neck and occipital region is complained of, and radiological examination has generally revealed some evidence of cervical arthritis, the region, however, chiefly affected is that of the fifth and sixth cervical vertebræ, a very common site in subjects of our predominant age group, and it has therefore been impossible to attribute any significance thereto."

While agreeing with this as a general statement, we do not think it applies to certain cases. The damaged otolith will produce vertigo depending upon the position of the head in space. We followed the instructions of Nylen (1950) to "prevent nystagmus through occlusion of the vertebral artery by compression or as a result of alteration in the cervical vertebral column." The head and spine were moved as a whole, and under these circumstances we were quite unable to produce vertigo or nystagmus in any of our cases; only when the head was allowed to move freely on the neck was the characteristic syndrome produced.

But why is vertigo rare whereas cervical arthritis is common? For reasons we shall discuss when we consider the mechanism of this condition, we believe it to depend on disease of the upper cervical spine only, which was the case in the four patients of ours in whom bony damage was demonstrated.

*Post-tractional Vertigo*

Several patients whom we have questioned have complained of dizziness and fainting after neck traction, and there is no doubt that the two patients we have described had attacks of vertigo.

Mayoux et al. refer to this condition when discussing the effect of neck traction in three cases, one of which clearly fits into our group:

"Mrs. S. presented with a neurological syndrome due to a cervical disc syndrome, she had never had vertigo . . . violent vertigo made its appearance [immediately after neck traction] and examination showed an intense nystagmus."

Watkyn-Thomas (1954), at the end of his summary of the article by Dix and Hallpike on vestibular neuronitis, says:

"It appears probable that in some of these cases the exciting cause may be an interference with neck reflexes . . . In some cases of Nuchal Myalgia postural vertigo may be induced and then abolished by manipulation."

*Post-traumatic Vertigo*

Gordon (1954) describes five cases (in many ways similar to our own) of vertigo following head injury. He considers that the vertigo was caused by otolith disease, and we have seen cases which we have classified in this group, but the otoliths were not at fault in our patients.

There were also other essential differences between our patients and Gordon's. In each of his cases the accident was severe with loss of consciousness lasting for several minutes, while consciousness was not lost in our first patient and in the other only very briefly. His cases showed other post-concussional symptoms, such as headache and irritability, while in our cases these were entirely absent. In his patients the symptoms had persisted for years; in ours they were of brief duration, with the exception of case 5, in whom they lasted for several months; but in this case there was radiographic evidence of damage to her cervical spine.

Both in our cases and in Gordon's the symptoms were relieved by wearing a collar, but this was to be expected whether the vertigo was due to the position of the head in space or to its position relative to the neck.

Finally, all our patients complained of pain in the neck and occiput, the site of injury.

### MECHANISM

*Occlusion of the Vertebral Artery*

de Kleyne and Nieuwenhuyse (1927) first suggested that nystagmus might be induced by occlusion of the vertebral artery when the head was held in certain positions.

Each vertebral artery gives rise to the posterior inferior cerebellar artery on its own side, and also to the anterior and posterior spinal arteries. The two arteries unite to form

the basilar artery, from which spring the posterior cerebral arteries (Schaeffer 1943).

Thus, occlusion of either vertebral artery would deprive the posterior inferior cerebellar artery on its own side of its blood-supply, and should therefore have wider effects.

Ford (1952) has described a case of short-lasting, recurrent obstruction to the vertebral arteries. A boy, aged 17, developed attacks of syncope followed by vertigo, nystagmus, and diplopia sometimes induced by forcing the head backwards. These were caused by a defect in the odontoid process, allowing an unusual degree of mobility in the second cervical vertebral joint. Ford also refers to two similar cases.

In our own cases the only abnormalities were vertigo and nystagmus; no wider involvement of the central nervous system or displacement of the vertebræ were ever demonstrated.

*Involvement of the Cervical Sympathetic System*

Barré (1926) held that the vertigo in his cases was a result of cervical osteo-arthritis involving the sympathetic system—a view supported by Mayoux et al. (1951). Neuwirth (1952) thought that the headache and facial pain in his cases were caused by a similar mechanism.

Yet it seems unlikely that stimulation of the sympathetic chain in the neck region sufficient to cause vertigo would not also give rise to more widespread manifestations. Barré says that 'Surocaine' injected at the base of the neck ("at the base of the vertebral nerves") produced tinnitus, vertigo, and nystagmus; but these symptoms may not have been caused by infiltration of the sympathetic fibres, nor would it explain the mechanism in Watkyn-Thomas's (1954) cases or in our own.

Finally, Cawthorne and Hewlett (1954), discussing vasodilatation and vasoconstriction in Ménière's disease, end by saying "all this suggests that much more work needs to be done before we can accept without question hypotheses concerning the effect of altering the blood flow through the labyrinth in Ménière's disease."

*Involvement of the Neck Reflexes*

We agree with Watkyn-Thomas (1954) that the cause of the vertigo in the cases we have described was interference with the tonic neck reflexes. Whether trauma, osteo-arthritis, neck traction, or injection of fluid is responsible, damage is done to the muscles and ligaments of the neck.

The centre for the neck reflexes is in the upper cervical region of the cord (Samson Wright 1952). The afferent impulses pass in the posterior roots of c1, 2, and 3, and come chiefly from the muscles of the back of the neck. This supports our contention that damage must be high in the cervical region to produce vertigo.

The actual paths by which proprioceptive impulses travel, and the nature of such impulses in man, is in doubt. However, many possible anatomical pathways have been demonstrated in animals. Jansen and Brodal (1954) refer to the following afferent cerebellar fibres:

(1) Ventral spinocerebellar tract.

(2) External cuneatecerebellar fibres from the cervical and upper thoracic spinal levels.

(3) Olivocerebellar fibres from all levels of the spinal cord.

(4) Reticulocerebellar fibres conveying impulses from the fore limb and hind limb and possibly from the neck also.

(5 and 6) Perihypoglossal and trigeminocerebellar fibres of unknown origin.

These findings are purely anatomical, mainly obtained by the method of retrograde degeneration, and only the primary endings of any one tract can be mapped out. Possibly an impulse originating in any spinal segment activates a larger part of the cerebellar cortex than is accounted for by anatomical studies.

Trauma to the neck causes an alteration in the proprioceptive impulses from the end-organs, but the pain and reactionary œdema which occur will, for a variable time, act as a splint to the neck. Subsequently, however, these will become less effective, particularly when the neck is relaxed as on lying down; and more stretching will occur, causing further alterations in the impulses reaching the cerebellum and vestibular nuclei. In the same way that false information reaching these centres from the diseased vestibule or otolith ultimately causes "consciousness of disordered orientation of the body in space" (Brain 1951), so will our class of patients experience vertigo associated with nystagmus. As the effect of the trauma subsides, increased stretching of the neck will be needed to induce vertigo, and the patient will have symptoms only on extreme movements, such as looking far upwards.

As the damage involves the peripheral end-organs only, no central signs will be found, and the vertigo can be expected to disappear when healing occurs, or when the brain adjusts itself to the defect.

## Conclusions

Disease of the neck is a not uncommon cause of vertigo in man, and we suggest that this syndrome be called cervical vertigo.

We have so far found three groups of patients who have this syndrome: (1) patients with cervical spondylosis; (2) patients treated by neck traction; and (3) patients with certain types of neck injury.

Such patients usually have pain in the back of the neck and occipital region, sometimes accompanied by stiffness of the neck. After a varying latent interval, recurrent postural vertigo, occurring on lying down and on bending the neck into certain positions, is noticed. This symptom may be reproduced, and nystagmus induced by bending the neck, but not by merely positioning the head in space. The prognosis is good, and relief may be obtained by wearing a cervical collar until the underlying lesion has resolved.

We should like to thank Dr. I. Calma, of the physiology department, University of Liverpool, for his help on the neck-reflex mechanisms; Dr. R. R. Hughes, of the Royal Southern Hospital, for permission to examine and describe two of his patients; and the registrars of the Liverpool Ear, Nose, and Throat Infirmary, for carrying out detailed auditory examinations.

REFERENCES

Barré, J. A. (1926) *Rev. neurol.* **1**, 1246.
Brain, W. R. (1951) Diseases of the Nervous System. London; p. 193.
— (1954) *Lancet*, **i**, 686.
Cawthorne, T., Hewlett, A. B. (1954) *Proc. R. Soc. Med.* **47**, 663.
de Kleyne, A., and Nieuwenhuyse (1927) *Acta otolaryng., Stockh.* **11**, 155.
Denny Brown, D. E. (1949) *New Engl. J. Med.* **241**, 144.
Dix, M. R., Hallpike, C. S. (1952) *Proc. R. Soc. Med.* **45**, 341.
Ford, F. R. (1952) *Bull. Johns Hopk. Hosp.* **91**, 168.
Gordon, N. (1954) *Lancet*, **i**, 1216.
Jansen, J., Brodal, A. (1954) Aspects of Cerebellar Anatomy. Oslo; chap. 2.
Mayoux, R., Girard, P., Chappaz, P. (1951) *Ann. Oto-laryng.* **68**, 705.
Neuwirth, E. (1952) *Ann. intern. Med.* **37**, 75.
Nylen, C. O. (1950) *J. Laryng.* **64**, 295.
*Proceedings of the Royal Society of Medicine* (1948) **41**, 509.
Schaeffer, J. P. (1943) Morris's Human Anatomy. Philadelphia; p. 633.
Symonds, C. (1952) *J. Laryng.* **66**, 295.
Watkyn-Thomas, F. W. (1954) *British Medical Annual*, p. 136.
Wildhagen, F. (1951) *Arch. Ohr.-, Nas.-, u. KehlkHeilk* **159**, 242.
Wright, S. (1952) Applied Physiology. London; p. 591.

"... there is a growing recognition that, in addition to learning factual knowledge and acquiring a certain degree of professional skill, the medical student is also acquiring a rich complex of attitudes and values that will often determine how he uses his skills and knowledge. What kinds of attitudes and values are involved, and where does he learn them? What is the influence of the informal structure of his environment as well as the formal structure of the curriculum? How do the student's interpersonal relationships with other students, faculty, and patients affect him? What are the similarities and dissimilarities of student response to the same teaching exercise or technique? How does the faculty view its job? These and many other questions must be explored in order to identify, and ultimately to understand, the critical factors in medical learning."—Annual report of the Commonwealth Fund, 1955, p. 7.

# DETERMINATION OF 5-HYDROXY-INDOLE-ACETIC ACID IN URINE AND ITS EXCRETION IN PATIENTS WITH MALIGNANT CARCINOIDS

ARNE HANSON
Chem. Eng.
FOLKE SERIN
M.D.
*From the Departments of Clinical Chemistry and Medicine, University of Lund, General Hospital, Malmö, Sweden*

ATTENTION was focused on metastatic malignant abdominal carcinoids ("carcinoidosis") by Waldenström (1954a) as the cause of a syndrome principally manifested by attacks of flushing, tachycardia, asthma, hyperperistalsis, and right-sided valvular disease of the heart (Waldenström and Ljungberg 1953, 1955, Thorson et al. 1954).

Lembeck (1953, 1954) and Ratzenhofer and Lembeck (1954) have shown that abdominal carcinoids contain large amounts of 5-hydroxytryptamine (enteramine, serotonin), and Pernow and Waldenström (1954) have found, in the blood and urine of patients with carcinoid during attacks of flushing, substances resembling 5-hydroxytryptamine in their biological effects.

Waldenström (1954a) suggests that this syndrome is caused by the release of 5-hydroxytryptamine into the blood from the tumour.

The discovery that 5-hydroxytryptamine is broken down by mono-amine oxidase (Blaschko 1952, Blaschko and Philpot 1953) and excreted in the urine as 5-hydroxy-indole-acetic acid (Erspamer 1954, 1955) made it very probable that the excretion of this metabolite would be increased in patients with malignant abdominal carcinoids. This effect has indeed been reported by Page et al. (1955) and Szoerdsma and Udenfriend (1955), who found a very large increase in the urinary excretion of 5-hydroxy-indole-acetic acid in such patients.

We have studied the excretion of 5-hydroxy-indole-acetic acid in 8 patients with carcinoid proved by microscopy, and followed the daily excretion of 5-hydroxy-indole-acetic acid in 2 of these patients, who were in the General Hospital, Malmö.

Early in our investigations we noticed that the urine from these patients became blue when treated with Ehrlich's aldehyde reagent (*p*-dimethylaminobenzaldehyde in dilute hydrochloric acid). It is well known that certain indole derivatives are turned blue by Ehrlich's aldehyde reagent, and this reaction has been used by Erspamer and Boretti (1951) to detect 5-hydroxy-tryptamine and other indole derivatives on paper chromatograms. It was therefore to be expected that patients with carcinoid would excrete large amounts of indole derivatives in their urine.

By paper chromatography we found that the indole derivatives excreted consisted almost exclusively of 5-hydroxy-indole-acetic acid. A qualitative and quantitative method for determining it, based on the reaction of indole derivatives to Ehrlich's aldehyde reagent, has been elaborated.

## Methods

*Paper Chromatography of Extracts of Urine*

The urine was extracted in the following way:

100 ml. of the 24-hour specimen was made alkaline to pH 8·5–9·0 with ammonia. The solution was filtered and extracted twice with 50 ml. of ether to remove impurities. The solution was next acidified to pH 4·0 with dilute hydrochloric acid and, after filtration, extracted three times with 100 ml. of ether. The pooled ether extracts were dehydrated with anhydrous sodium sulphate and evaporated to dryness in vacuo. The residue was dissolved in ethanol and used for chromatography.

Paper chromatography was done by the method of Erspamer (1955) with a solvent mixture of *n*-butanol + acetic acid + water (4 : 1 : 5). For developing the spots the paper was sprayed by the method of Erspamer and Boretti (1951) with either an alcoholic solution of *p*-dimethylaminobenzaldehyde or a solution of 2-chloro-4-nitrobenzenediazoniumnaphthalenesulphonate in dilute hydrochloric acid.

*Qualitative Determination*

Urine from patients with carcinoid is turned blue by Ehrlich's aldehyde reagent, and this reaction may be used as a screen-test in most cases of carcinoidosis. The test may be applied direct to the sample of urine. Preferably 3 ml. of Ehrlich's aldehyde reagent is added to 3 ml. of urine and boiled. The blue colour may sometimes be rather faint when the concentration of 5-hydroxy-indole-acetic acid is low or there is much interference by urinary or other pigments. In such cases it is better to apply the test to the residue obtained by extracting the acidified urine with ether.

*Quantitative Determination*

2 ml. of filtered urine is acidified with one or two drops of 10% hydrochloric acid and extracted twice with 25 ml. of ether in a small separating funnel. The pooled ether extracts are filtered, dehydrated with about 3 g. of anhydrous sodium sulphate, and evaporated to dryness at 50°C in a water-bath. The residue is dissolved in 1 ml. of 0·1 *N* hydrochloric acid, and to 0·2 ml. of this solution in a test-tube is added 5 ml. of Ehrlich's aldehyde reagent. The solution and a blank consisting of 0·2 ml. of 0·1 *N* hydrochloric acid and 5 ml. of Ehrlich's reagent are then heated for 2 hours in a water-bath at 45–50°C, whereupon the test solution becomes blue. The solutions are next removed from the water-bath and immediately diluted with cold 50% ethyl alcohol to 10 ml. The colour is measured with a spectrophotometer (Beckman DU) at 590 mμ. Extinction × 62·5 = mg. of 5-hydroxy-indole-acetic acid per 100 ml. of urine. When the test is done as described here, the Lambert-Beer law is obeyed within a concentration range of 0–20 mg. of 5-hydroxy-indole-acetic acid per 100 ml.

This method allows a determination of 5 μg. of 5-hydroxy-indole-acetic acid (12·5 mg. per 1000 ml. of urine). If the blue is too faint to read, the test should be repeated on a larger volume of the hydrochloric-acid solution—e.g., the remaining 0·8 ml. In the present cases of carcinoid 0·2 ml. was sufficient for all the determinations.

## Material

The specimens of urine tested in this investigation came from 7 patients with malignant carcinoid proved by microscopy and from 1 patient whose symptoms subsided after surgical removal of a carcinoid tumour.

## Case-reports

The relevant details of the 2 patients admitted to this hospital are as follows:

**Case 1.**—A male factory worker, aged 57, had been healthy until eight years ago, when he had recurrent attacks of epigastric pain. During the last two years he had observed a patchy flush. At first the flush came on after he drank alcohol but later it appeared spontaneously. He was admitted to hospital a year ago because of abdominal discomfort and diarrhœa. Six months ago enlargement of the liver and a murmur over the lower part of the sternum were detected. A few months later he was readmitted to hospital, and attention was drawn to the carcinoid syndrome. The patient's urine and blood contained high concentrations of a substance resembling 5-hydroxytryptamine. He was then referred to this hospital with the diagnosis of malignant carcinoid. The urinary excretion of 5-hydroxy-indole-acetic acid is shown in fig. 1. During his stay here he had an intestinal perforation and had to be transferred to the surgical side, and the opportunity was taken to prove the diagnosis by biopsy. Later he had another intestinal perforation and died. Necropsy

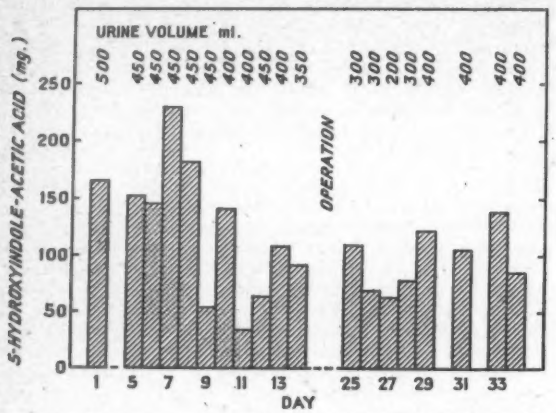



Fig. 1—Urinary excretion of 5-hydroxy-indole-acetic acid in case 1.

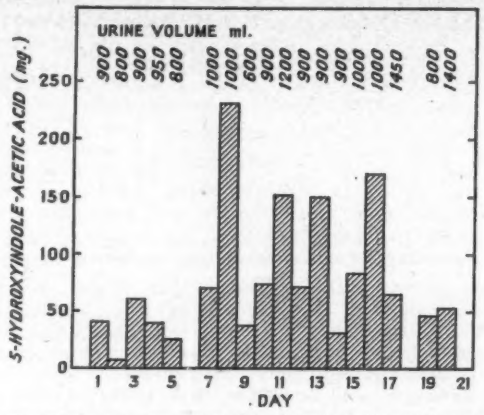



Fig. 2—Urinary excretion of 5-hydroxy-indole-acetic acid in case 2.

revealed pulmonary stenosis and a carcinoid in the small intestine with extensive metastases in the mesentery and the liver.

**Case 2.**—A woman, aged 57, with ten years' history of attacks of abdominal pain and four years' history of attacks of ileus, was operated on about three years ago, when a carcinoid tumour of the small intestine was found with metastases in the mesentery. Postoperatively she had intermittent attacks of pain, diarrhœa (as much as twenty loose stools a day), and flushes, which appeared especially when she drank alcohol or became excited. Three months ago enlargement of the liver and a loud systolic murmur over the lower left part of the sternum were noted. During the past two years her urine has intermittently been red. The urinary excretion of 5-hydroxyindole-acetic acid is shown in fig. 2.

## Results

Besides cases 1 and 2 we examined single samples of urine from 5 other patients with carcinoid and found in all of them 5-hydroxy-indole-acetic acid by the qualitative test. By paper chromatography this substance was found to be the major metabolite. In none of the cases was either 5-hydroxytryptamine or tryptamine detected in the urine.

Urine from a patient whose symptoms of carcinoidosis had disappeared after surgical removal of a carcinoid tumour gave a negative reaction.

In 3 of the above-mentioned patients the urine was red and contained rather large amounts of red pigments which probably arose from the increased metabolism of 5-hydroxytryptamine. The pigments appear, however, intermittently in the urine, and their formation seems to depend on the interplay between several factors. Increased excretion of 5-hydroxy-indole-acetic acid alone is insufficient to produce the pigments. These pigments and the mechanism of their formation are at present being studied by one of us (A. H.).

## Discussion

Paper chromatography was done by the techniques described by Clerc-Bory et al. (1954) and Erspamer (1955). Of different solvents tried we found a mixture of *n*-butanol + acetic acid + water to give a good separation, and this solvent was therefore chosen for most of our analyses. The fact that 5-hydroxy-indole-acetic acid always predominated and very often was the only detectable metabolite led us to regard the use of further solvents as unnecessary (cf. Erspamer 1955).

An approximate estimation of 5-hydroxy-indole-acetic acid in extracts of urine and blood has hitherto usually been made either by simple visual examination of the spots on the paper chromatograms—i.e., comparison, as regards area and density of colour, of the spot given by the extract and spots obtained with known amounts of 5-hydroxy-indole-acetic acid, or by elution of this substance from the paper chromatograms and subsequent colorimetric determination in the eluate. Neither of these procedures is, however, very suitable for clinical work: the former may be subject to large errors in judgment and requires a great many repeated analyses at various dilutions to give reasonably satisfactory results; and the latter, though more accurate, is very laborious and time-consuming and requires considerable analytical skill.

A specific colorimetric procedure for measuring 5-hydroxy-indole-acetic acid in urine, based on a reaction with α-nitroso-β-naphthol, has been developed by Udenfriend and Titus (1955); but details of it have not yet been published.

We developed a simple method for the quantitative determination of 5-hydroxy-indole-acetic acid directly in urine. The method is not specific for 5-hydroxy-indole-acetic acid; several other indole derivatives—e.g., 5-hydroxytryptamine and tryptamine—give a similar reaction. However, this does not limit the applicability of the method, because paper chromatography has shown that 5-hydroxyindole-acetic acid is the predominant metabolite.

The copious excretion of 5-hydroxyindole-acetic acid in the urine—up to 230 mg. in twenty-four hours—shows that patients with malignant carcinoid metabolise enormous amounts of 5-hydroxytryptamine. The normal excretion of 5-hydroxy-indole-acetic acid in twenty-four hours has been reported as 4·5 mg. (Erspamer 1955), 10 mg. (Titus and Udenfriend 1954), and 3–8 mg. (Szoerdsma and Udenfriend 1955). These normal values are all so low as not to be detected by the above-mentioned screen-test. The quantitative method is, however, applicable even down to these small amounts.

The excretion of 5-hydroxy-indole-acetic acid in patients with carcinoid usually largely exceeds the reported normal values. On one occasion, however, in 1 of our patients it was as low as 6 mg. in twenty-four hours. In the investigation of suspected cases of carcinoid the urine should therefore be examined repeatedly. A single negative result may give rise to false conclusions.

Malignant carcinoids should probably be classed with tumours which are characterised by increased hormonal activity—e.g., phæochromocytoma and chorionepithelioma (cf. Waldenström 1954 a and b). The presence of a specific metabolite in the urine—in this case 5-hydroxy-indole-acetic acid—and its identification should be of great value in diagnosis, which could of course also be confirmed by finding an increased amount of 5-hydroxytryptamine in the blood. The identification of 5-hydroxy-indole-acetic acid in the urine—which reflects the metabolism of 5-hydroxytryptamine—is, however, much easier from a technical point of view.

Continuous observation of the urinary excretion of 5-hydroxy-indole-acetic acid after surgical removal of a malignant carcinoid should be of help in assessing the effectiveness of therapy.


### Summary

A screen-test suitable for rapid examination of suspected cases of carcinoid is described.

A simple method for the quantitative determination of 5-hydroxy-indole-acetic acid in urine has been developed.

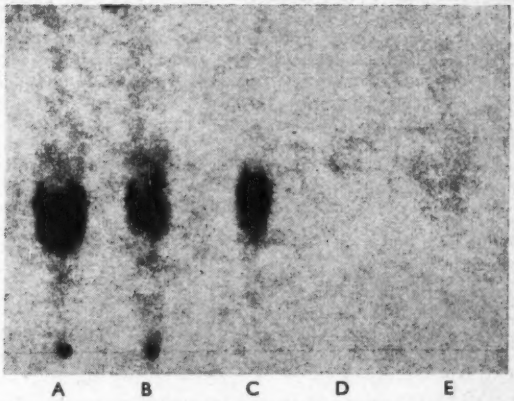
The urinary excretion of 5-hydroxy-indole-acetic acid has been followed in 2 patients with malignant abdominal carcinoid (carcinoidosis).

An abnormally large amount of 5-hydroxy-indole-acetic acid was found in the urine of 5 other patients.

In a 6th case no abnormally large amount of urinary 5-hydroxy-indole-acetic acid was found after surgical ablation of a carcinoid tumour.

Paper chromatography has shown that that 5-hydroxy-indole-acetic acid is the predominant metabolite of 5-hydroxy-tryptamine.

In 3 of the patients with carcinoidosis the urine contained red pigments, probably arising from the increased formation of 5-hydroxy-indole-acetic acid.


**Chromatogram run for 45 min. in sodium-chloride/acetic-acid solution, Whatman no. 4 paper.**

A, B = 50 µl. urine of patients with metastasising carcinoid.
C = 5 µg. 5-H.I.A.A.
D, E = 50 µl. urine of healthy people.
Urea, indoxyl sulphate, tryptophan, and indole-acetic acid do not show in the figure.


REFERENCES

Blaschko, H. (1952) *Pharmacol. Rev.* **4**, 415.
— Philpot, F. J. (1953) *J. Physiol.* **122**, 403.
Clerc-Bory, M., Pacheco, H., Mentzer, C. (1954) *C.R. Acad. Sci., Paris*, **238**, 525.
Erspamer, V. (1954) *Pharmacol. Rev.* **6**, 425.
— (1955) *J. Physiol.* **127**, 118.
— Boretti, G. (1951) *Arch. int. Pharmacodyn.* **88**, 296.
Lembeck, F. (1953) *Nature, Lond.* **172**, 910.
— (1954) *Arch. exp. Path. Pharmak.* **221**, 50.
Page, I. H., Corcoran, A. C., Udenfriend, S., Szoerdsma, A., Weissbach, H. (1955) *Lancet*, i, 198.
Pernow, B., Waldenström, J. (1954) *Ibid*, ii, 951.
Ratzenhofer, M., Lembeck, F. (1954) *Z. Krebsforsch.* **60**, 169.
Szoerdsma, A., Udenfriend, S. (1955) *J. clin. Invest.* **34**, 914.
Thorson, Å., Björck, G., Björkman, G., Waldenström, J. (1954) *Amer. Heart J.* **47**, 795.
Titus, E., Udenfriend, S. (1954) *Fed. Proc.* **13**, 411.
Udenfriend, S., Titus, E. (1955) *In* McElroy, W. D., Glass, H. B. A Symposium on Amino Acid Metabolism. Baltimore; p. 948.
Waldenström, J. (1954a) *Nord. Med.* **51**, 891.
— (1954b) *Acta endocr., Copenhagen*, **17**, 432.
— Ljungberg, E. (1953) *Sv. Läkartidn.* **50**, 690.
— — (1955) *Acta med. scand.* **152**, 293, 311.


## A RAPID CHROMATOGRAPHIC TEST FOR HIGH URINARY EXCRETION OF 5-HYDROXY-INDOLE-ACETIC ACID AND 5-HYDROXYTRYPTAMINE


G. CURZON
B.Sc., Ph.D. Leeds

SCHLESINGER RESEARCH FELLOW, THE NATIONAL HOSPITAL FOR NERVOUS DISEASES, QUEEN SQUARE, LONDON


HIGH urinary output of 5-hydroxy-indole-acetic acid (5 H.I.A.A.) is probably the most useful biochemical indication of metastasising carcinoid tumours (Page et al. 1955, Szoerdsma and Udenfriend 1955, Snow et al. 1955, Goble et al. 1955). 5-hydroxytryptamine (5-H.T.) excretion has also been found to be high in this disease (Pernow and Waldenström 1954, Snow et al. 1955).

5-H.I.A.A. may be determined quantitatively by a colorimetric method (Udenfriend et al. 1955) or qualitatively and semi-quantitatively by various chromatographic methods (Jepson 1955, Snow et al. 1955). A simple qualitative test based on the colorimetric method has recently been described (Szoerdsma et al. 1955).

The following rapid test, which has been used in the study of suspected cases of metastasising carcinoid, is based on paper chromatography using sodium-chloride/acetic-acid solutions. Inorganic salt solutions have previously been used by Boscott (1952) as chromatographic solvents, mainly in the separation of phenolic acids, and by Horne and Pollard (1948) in the chromatography of streptomycin.

### Method

*Apparatus*

No special apparatus is needed. Chromatograms may be conveniently run in wide-necked screw-top jars using Whatman no. 4 paper for preference.

*Chromatographic solvents*

For the detection of 5-H.T.: 8 g. sodium chloride dissolved in 100 ml. water.

For the detection of 5-H.I.A.A.: 8 g. sodium chloride dissolved in 100 ml. water + 1·0 ml. glacial acetic acid.

*Colour Reagent*

2 g. dimethylaminobenzaldehyde is dissolved in 5 ml. concentrated hydrochloric acid and 95 ml. water is added.

*Procedure*

50 µl. urine is applied at a point 4 cm. from an edge of a rectangular piece of Whatman no. 4 paper. (Occasionally very concentrated urines give satisfactory chromatograms only when 25 µl. is used.) The urine is applied in 10 µl. portions from a micro-pipette and dried by a warm-air current. 5 µl. of a 1 mg. per ml. ethanolic solution of 5-H.I.A.A. or of a 0·2 mg. per ml. aqueous solution of 5-H.T. may be applied in parallel with the urine spot and also a normal urine for comparison. The sheet is fastened in cylindrical form with staples and stood for 45 min. in about 100 ml. solvent in a wide-necked jar. During this time the solvent travels about 15 cm. The chromatogram is then dried in a warm-air oven, sprayed with the colour reagent, and heated at 55–60°C for 10–15 min.

### Results

After colour development, normal urine chromatograms show a strong yellow urea spot and often weak spots in the indoxyl-sulphate, tryptophan, and indole-acetic-acid positions. This pattern was shown by 110 urines of healthy people. Urines containing at least 20 mg. per litre of 5-H.I.A.A. show a further blue-grey spot which tends to become stronger on standing (see figure). This travels separately from all the other indole material

present using sodium-chloride/acetic-acid as solvent. Urines containing at least 2 mg. per litre of 5-H.T. show a blue spot running separately from other indoles present, in the sodium-chloride solvent. This spot fades on standing. Urines from all 9 reported cases of metastasising carcinoid on which 5-H.I.A.A. determinations have been done contained 5-H.I.A.A. at a level well above the limit of sensitivity of the test, with the exception of case 3 of Snow et al. (1955), in which urinary 5-H.I.A.A. levels of 6·8–44 mg. per litre were found. In this case, however, the urinary 5-H.T. level was high enough to be easily detected. Case 1 of Snow et al. excreted very large amounts of 5-H.I.A.A. but amounts of 5-H.T. which, though gross in comparison with normals, were usually below the limits of sensitivity of the chromatographic test.

The solvents used may perhaps be found of more general use. $R_f$ values of some of the more common indole substances are shown in the accompanying table.

$R_f$ VALUES AND COLOUR REACTIONS OF COMMON INDOLE SUBSTANCES

| Substance | Approximate $R_f$ | | Colour with dimethylamino-benzaldehyde reagent | |
|---|---|---|---|---|
| | Sodium chloride | Sodium-chloride/acetic-acid | After 10 min. at 60°C | On standing |
| Urea .. .. .. | 0·80 | 0·84 | Yellow | Yellow |
| 5-H.I.A.A. .. .. .. | 0·55 | 0·42 | Blue-grey | Blue |
| 5-H.T. .. .. .. | 0·34 | 0·37 | Blue | Fades |
| Indole-acetic acid .. | 0·71 | 0·54 | Purple | Fades |
| Indoxyl sulphate .. | 0·63 | 0·65 | Orange | Orange |
| Tryptophan .. .. | 0·54 | 0·55 | Purple | Fades rapidly |
| Tryptamine .. .. | 0·48 | 0·54 | Purple | Fades |
| 5-hydroxytryptophan .. | 0·41 | 0·40 | Blue | Fades rapidly |
| 5-H.I.A.A. sulphate .. | 0·75 | 0·66 | Blue-grey | Blue |
| Bufotenine .. .. | 0·49 | 0·49 | Blue | Fades |

These refer to the pure substances; in the presence of urine there may be slight retardation of the spots.

## Conclusion

This method may prove useful in the diagnosis of metastasising carcinoid. Results are obtainable in little more than an hour. The chemical substances needed are to be found in any clinical laboratory. Mephenesin (G. Curzon, unpublished) and acetanilide and related drugs interfere with the test of Szoerdsma et al. (1955) but are without effect on the test described here.

Possibly cases may be found in which the clinical signs point to metastasising carcinoid though urinary 5-H.I.A.A. and 5-H.T. excretion are below the limits of sensitivity of the test. Should this occur, it would be necessary to determine urinary 5-H.I.A.A. quantitatively, as mg. 5-H.I.A.A. per g. creatinine or per 24-hr. excretion.

I thank Dr. J. N. Cumings for laboratory facilities and the Upjohn Company for samples of 5-H.I.A.A. and 5-H.T.

### REFERENCES

Boscott, R. J. (1952) *Chem. & Ind.* p. 472.
Goble, A. J., Hay, D. R., Sandler, M. (1955) *Lancet*, ii, 1016.
Horne, R. E., Pollard, A. (1948) *J. Bact.* **55**, 231.
Jepson, J. B. (1955) *Lancet*, ii, 1009.
Page, I. H., Corcoran, A. C., Udenfriend, S., Szoerdsma, A., Weissbach, H. (1955) *Ibid*, i, 198.
Pernow, B., Waldenström, J. (1954) *Ibid*, ii, 951.
Snow, P. J. D., Lennard-Jones, J. E., Curzon, G., Stacey, R. S., (1955) *Ibid*, ii, 1004.
Szoerdsma, A., Udenfriend, S. (1955) *J. clin. Invest.* **34**, 914.
— Weissbach, H., Udenfriend, S. (1955) *J. Amer. med. Ass.* **159**, 397.
Udenfriend, S., Weissbach, H., Clark, C. T. (1955) *J. biol. Chem.* **215**, 337.

# PRECIPITATION BY FATTY FOOD OF SYSTEMIC DISTURBANCE FROM ARGENTAFFINOMA

N. M. BLEEHEN
M.A., B.Sc., B.M. Oxfd
HOUSE-OFFICER, MEYERSTEIN INSTITUTE OF RADIOTHERAPY, THE MIDDLESEX HOSPITAL, LONDON

SOME patients with intestinal argentaffin carcinoma have paroxysmal attacks of flushing, dyspnœa, and diarrhœa; and such attacks have been related to the secretion by the tumour mass of 5-hydroxytryptamine (5-H.T.). Factors which have been found to precipitate attacks include emotion, spices, and food (Thorson et al. 1954), and alcohol (Snow et al. 1955); but in most cases no precipitating factor has been recognised. It has been suggested that 5-H.T. may have a physiological rôle in intestinal activity.

In the present case attacks were consistently provoked by a diet with a high-fat content.

A housewife, aged 64, was admitted to hospital in August, 1955, with a four-year history of flushing attacks after eating a fatty cooked meal. Five to fifteen minutes after eating such food, which she had learnt to avoid when possible, her eyes would become blood-shot and for two to three minutes her vision would be blurred. She would then flush a bright pink, especially over her hands, feet, and face; and her lips, always slightly cyanosed, would become purple and swollen. At the same time she would feel breathless and have palpitations. These attacks lasted for about fifteen minutes; and for the past six months they had been associated with diarrhœa, which persisted for twenty-four hours. In 1953 examination had shown that her liver was enlarged to two inches below the costal margin, and a subcutaneous nodule, 2 mm. in diameter, had been found on the front of her chest. On admission in August, 1955, she had a permanent purple telangiectasia of the nose and malar region, ascites, sacral and ankle œdema, and an increased number of subcutaneous nodules on the trunk. There was no evidence of valvular disease of the heart. Radiography after a barium enema revealed an annular constriction in the lower third of the sigmoid colon, which was also seen at sigmoidoscopy. Since the epithelium was intact the surgeon did not regard biopsy as justifiable. A diagnosis of metastatic argentaffin carcinoma was confirmed by histological examination of two of the subcutaneous nodules, which showed carcinoma with the characteristic argentaffin-cell granules.

URINARY EXCRETION OF 5-HYDROXY-INDOLE-ACETIC ACID

| — | Day | | | |
|---|---|---|---|---|
| | 1 | 2 | 3* | 4 |
| Urine volume (ml.) .. | 840 | 900 | 550 | 1000 |
| 5-H.I.A.A. (mg. per day) .. | 80 | 90 | 200 | 70 |

* Fat meal given.

*Investigations.*—When the patient had been free from flushings for some days, the platelet-free plasma contained less than 0·02 µg. of 5-H.T. per ml., and the cerebrospinal fluid contained no detectable 5-H.T. or 5-hydroxy-indole-acetic acid (5-H.I.A.A.). These determinations were made chromatographically (Jepson 1955). Daily determinations of urinary 5-H.I.A.A. while the patient was on a low-fat diet (about 30 g. per day) showed an excretion of 70–90 mg. per day; in this period there were no paroxysmal attacks. After a cooked meal containing 70 g. of fat, which induced mild flushing and severe diarrhœa, the 5-H.I.A.A. excretion was more than doubled for that day, returning to the previous level on the following day (see table).

These results are reported because of their possible physiological interest, in that the stimulus to the secretion of 5-H.T. by the argentaffin carcinoma in this case is a normal constituent of food.

I wish to thank Miss M. D. Snelling and Dr. G. E. Beaumont for permission to publish this case; Dr. J. B. Jepson, of the

Courtauld Institute of Biochemistry, Middlesex Hospital Medical School, for the estimations of 5-H.T. and 5-H.I.A.A. and for much helpful advice; and Dr. A. D. Thomson, of the Bland Sutton Institute of Pathology, Middlesex Hospital Medical School, for reporting on the biopsy specimens.

REFERENCES

Jepson, J. B. (1955) *Lancet*, ii, 1009.
Snow, P. J. D., Lennard-Jones, J. E., Curzon, G., Stacey, R. S. (1955) *Ibid*, p. 1004.
Thorson, A., Biork, G., Björkman, G., Waldenström, J. (1954) *Amer. Heart J.* 47, 795.

# A BRITISH TARGET-CELL ANÆMIA

M. C. G. ISRAËLS
M.Sc., M.D. Manc., F.R.C.P.
LECTURER IN HÆMATOLOGY IN THE UNIVERSITY OF MANCHESTER

R. L. TURNER
M.B. Belf.
REGISTRAR

*From the Department of Hæmatology, Manchester Royal Infirmary*

THE presence of target-cells in the peripheral blood is classically associated with Mediterranean anæmia (thalassæmia, Cooley's syndrome) in patients with Italian, Sicilian, Greek, or other Levantine parentage. Both severely affected patients and those who have only the "trait" have target-cells in the blood. The cells are thinner than normal, and the osmotic fragility of the red cells is decreased. In Mediterranean anæmia a relatively large proportion of the hæmoglobin is of the fœtal type. In severe anæmia (thalassæmia major) the red cells have a shortened life-span, whereas in the trait (thalassæmia minor) the life-span is probably normal (Dacie 1954). The only other inherited anomaly of the red cells among which target-cells occur in the peripheral blood is that associated with the presence of hæmoglobin C (Neel et al. 1953). Target-cells can sometimes be found in the peripheral blood of patients with infective hepatitis or other liver diseases; Dacie et al. (1953) report one such case.

The two cases described here presented with a mild anæmia that did not respond to treatment. The patients had target-cells and ovalocytes in their blood, and similar cells were found in the blood of some of their relations. The alkali denaturation test showed that both patients had fœtal hæmoglobin still present in their blood. But the patients were not ill with gross splenomegaly like patients with typical Mediterranean anæmia, and there is no evidence of Mediterranean ancestry in either patient.

## Case-reports

**Case 1.**—A young woman, aged 24, who worked in a hospital laboratory, complained of feeling unusually tired. A blood-count showed her hæmoglobin to be only 10·5 g. per 100 ml., and she admitted that she had been "always anæmic." She was referred to the medical outpatient clinic. No abnormal physical signs other than pallor and slight icterus were found, and she was admitted for investigation.

*On examination* little unusual was found; she was rather pale and had slight but definite icterus, no enlargement of liver or spleen, and nothing abnormal in the other systems.

*Investigations.*—A blood-count showed red cells 4,473,000 per c.mm., Hb 10·8 g. per 100 ml., white cells 7300 per c.mm. (polymorphs 51%, lymphocytes 37%, monocytes 10·5%, eosinophils 0·5%, basophils 1%), reticulocytes 0·5%, and mean corpuscular Hb concentration (M.C.H.C.) 29%. Blood-films showed that target-cells and ovalocytes were regularly present (fig. 1). The sternal marrow showed a normal active picture with normal erythroblasts. The osmotic-fragility curve (fig. 2) showed definitely increased resistance to hypotonic saline solution; in a 0·4% sodium-chloride solute there was only 5% hæmolysis, in 0·32% there was still only 50%. Electrophoresis of the Hb was done on paper strips (35 × 5 cm. of Whatman 3MM paper) in a Durrum type of electrophoresis chamber; a sodium-barbitone buffer of pH 8·6, ionic concentration 0·05M, was

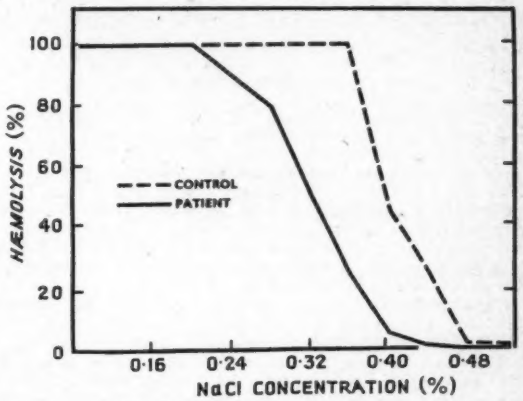



Fig. 2—Osmotic-fragility curve of case 1.

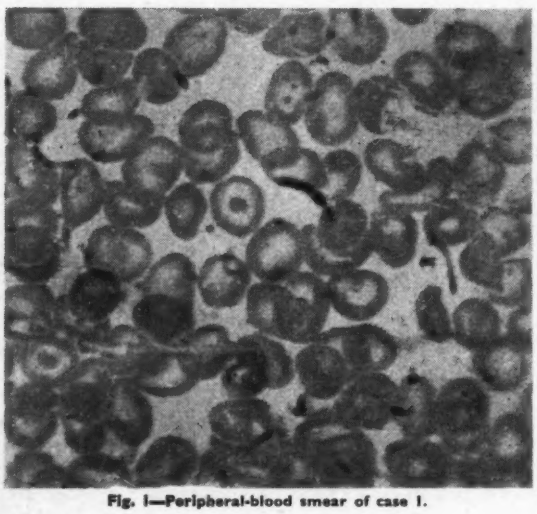


Fig. 1—Peripheral-blood smear of case 1.

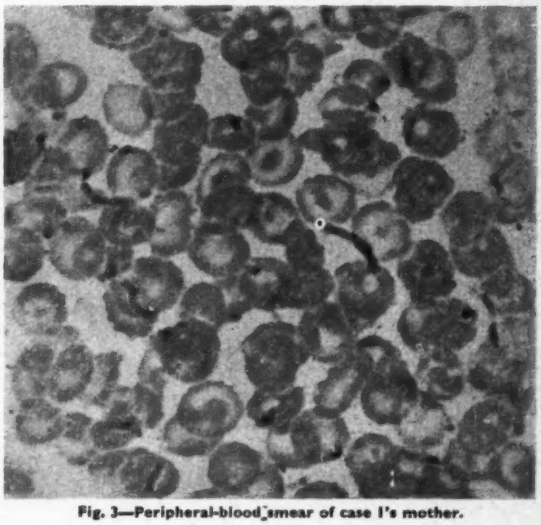


Fig. 3—Peripheral-blood smear of case 1's mother.

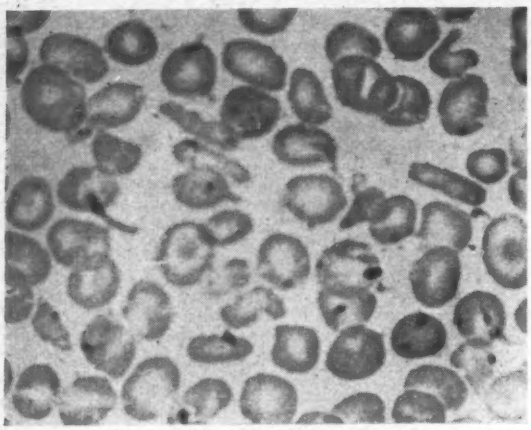


Fig. 4—Peripheral-blood smear of case 2.

used; 120V was applied for $17^1/_2$ hr. By this technique the hæmoglobin gave an entirely normal pattern. The alkali denaturation test by the technique of Singer et al. (1951) gave a one-minute reading of 5·4%, whereas normal values for adult blood in our laboratory have never exceeded 1·8%; the presence of fœtal Hb was therefore established. The serum-bilirubin level was persistently 1·0–1·7 mg. per 100 ml.; liver-function tests were normal; the Coombs anti-globulin test was negative. A test-meal showed normal acid secretion. No occult blood was present in the stools.

*Treatment.*—The patient was treated with full doses of oral and intravenous iron and adequate ascorbic acid. None of this had any effect on the Hb level.

*Family.*—The patient had no siblings. Her father was said to be quite healthy. Only her mother was available for testing, and she admitted to "anæmia" for many years. Her blood showed the same anomalies as those found in her daughter (fig. 3), and her Hb was 11·5 g. per 100 ml.

**Case 2.**—A young nurse, aged 23, had been pale while training. Eighteen months previously, while working as a staff nurse, her Hb was 10·1 g. per 100 ml. Her anæmia was investigated, but no cause was found. She was treated with oral and intravenous iron, vitamin $B_{12}$, folic acid, and small doses of thyroid, all without effect. Since she felt quite well and presented no pathological signs apart from a low Hb level, no further action was taken. Later, however, she married, and the question of her fitness for a pregnancy arose. She was therefore admitted to Manchester Royal Infirmary for reinvestigation.

*On examination* she was slightly pale but otherwise quite healthy, without any abnormal clinical signs in any of the systems except the blood.

*Investigations.*—A blood-count showed red cells 4,820,000 per c.mm., Hb 10·7 g. per 100 ml., white cells 6200 per c.mm. (polymorphs 78%, lymphocytes 18%, monocytes 4%), normoblasts 2 per 200 white cells, and reticulocytes 0·6%. A stained smear showed many target-cells and ovalocytes, considerable anisocytosis and poikilocytosis, and some stipple cells; the target-cells were mostly well shaped and regular (fig. 4). The sternal marrow was very cellular, with all types except lymphocytes increased; there was striking normoblastic hyperplasia, and some pro-erythroblasts and some double and triple nucleated normoblasts were present. The M.C.H.C. was 31%. The osmotic-fragility curve (fig. 5) showed strikingly increased resistance to hypotinic saline solution: there was only 5% hæmolysis in 0·4% sodium chloride and only 60% in 0·26% sodium chloride. Electrophoresis of the Hb under the same conditions as in case 1 gave a normal pattern, but again the alkali denaturation test showed the presence of fœtal Hb, the one-minute reading being 3·1%. The serum-bilirubin level was 0·4 mg. per 100 ml., serum-iron 220 µg. per 100 ml. (rather high), serum-albumin level 4·5 g. per 100 ml., and serum-globulin level 3·5 g. per 100 ml., with normal electrophoretic

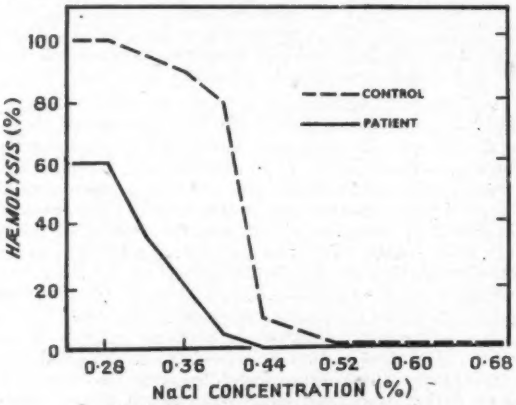



Fig. 5—Osmotic-fragility curve of case 2.

pattern. The Coombs anti-globulin test was negative. A test-meal showed normal acid secretion. No occult blood was found in the stools.

*Family.*—With the help of Dr. J. Steven Faulds, of Carlisle, the patient's family were investigated. Her father had normal red cells and Hb 16·9 g. per 100 ml.; her mother was anæmic, with Hb 9·4 g. per 100 ml. and target-cells in her blood (fig. 6); her sister, aged 20, was not anæmic, with Hb 12·7 g. per 100 ml., but had target-cells in her blood (fig. 7); and her brother, aged 8 years, was anæmic, with Hb 10·7 g. per 100 ml. and target-cells in his blood (fig. 8).

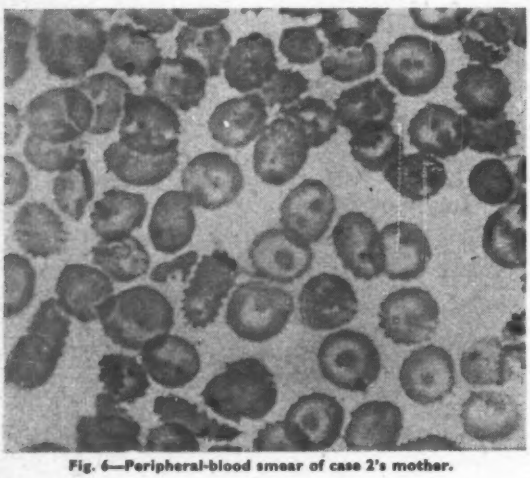


Fig. 6—Peripheral-blood smear of case 2's mother.

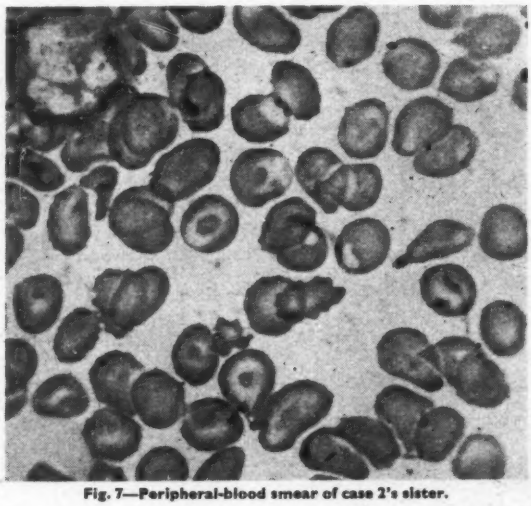


Fig. 7—Peripheral-blood smear of case 2's sister.

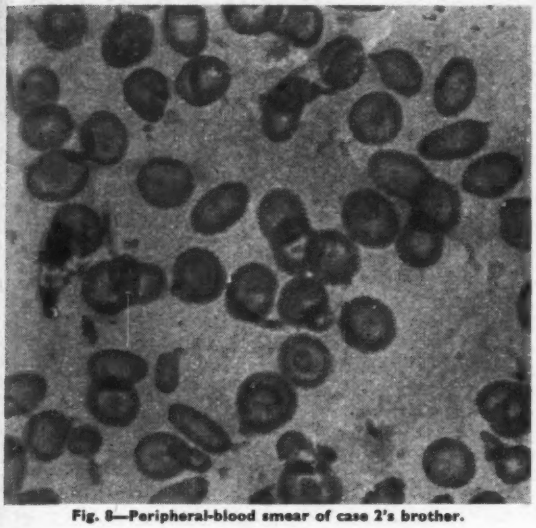


Fig. 8—Peripheral-blood smear of case 2's brother.

## Discussion

The clinical picture presented by these two young women was one of mild anæmia (Hb just under 11 g. per 100 ml.) causing them little disability, and their anæmia might well have passed unnoticed had they not been working in hospitals. They had no jaundice, no splenomegaly, and no hepatomegaly. Efforts to improve their Hb levels by giving hæmatinics failed completely. Examination of their peripheral blood showed the constant presence of target-cells and some ovalocytes. Their red cells showed a notably increased resistance to hypotonic saline solution. Electrophoresis of their Hb showed no abnormality; in particular there was no Hb C. The alkali denaturation test showed that fœtal Hb was present in excess in both patients. They had slight evidence of increased hæmolysis; one of them had a persistently raised serum-bilirubin level, and the other had a few normoblasts and stippled cells in the blood. Neither patient had any evidence of parenchymatous liver disease. The fact that other members of the families, including a brother of case 2, also had target-cells in their blood indicates that the condition falls into the group of inherited red-cell anomalies.

There is no question of Mediterranean ancestry in either family; and, although target-cells and fœtal Hb were present in their blood, clinically the condition differed from Mediterranean anæmia. None of the other red-cell anomalies described fit these two families. No Hb C was detected. In one of the families described by Rundles and Falls (1946) some target-cells were present and the osmotic resistance of the red cells showed some increase in that the curve extended beyond the normal limits; but their patients had splenomegaly. In Crosby's (1950) patients with "hereditary non-spherocytic hæmolytic anæmia" a very occasional target-cell was found, but otherwise the patients were quite different. None of the twelve patients with atypical congenital hæmolytic anæmia described by Dacie et al. (1953) showed either a clinical or a hæmatological picture like these two families with target-cell anæmia. The target-cell anæmia exemplified by these two families thus seems to be one more type to add to the list of inherited red-cell abnormalities, and clinically it resembles ovalocytosis more than the other, severer, syndromes.

The fact that target-cells were a diagnostic feature of the peripheral blood smears in these patients reinforces Dacie's warning that the presence of target-cells is *not* diagnostic for Mediterranean anæmia or trait.

When the nature of the anæmia was appreciated, all attempts at "treatment" were stopped. There is no reason to suppose that a Hb level of about 70% of average normal is a handicap to persons who are accommodated to it; many patients with more severe hereditary anæmias become accustomed to lower levels than this.

## Summary

Two cases are described of a mild target-cell anæmia unaccompanied by splenomegaly or other clinical signs; the patients were not of Mediterranean ancestry.

The same anomaly was found in some of the patients' relations.

Fœtal Hb was found in the patients' blood, but no other abnormal Hb.

This condition appears to be one more type of inherited red-cell anomaly.

Attempts to raise the Hb level by treatment are fruitless and should be discouraged.

The two patients were studied in the Manchester Royal Infirmary, case 1 being under the care of the late Dr. Norman Kletts and case 2 under that of Dr. John F. Wilkinson. We are much indebted also to Dr. Steven Faulds, of Carlisle, for information about case 2 and for obtaining specimens of blood from her family.

### REFERENCES

Crosby, W. H. (1950) *Blood*, **5**, 233.
Dacie, J. V. (1954) The Hæmolytic Anæmias. London; p. 126.
— Mollison, P. L., Richardson, N., Selwyn, J. G., Shapiro, L. (1953) *Quart. J. Med.* **22**, 79.
Neel, J. V., Kaplan, E., Zuelzer, W. W. (1953) *Blood*, **8**, 724.
Rundles, R. W., Falls, H. F. (1946) *Amer. J. Med. Sci.* **211**, 641.
Singer, K., Chernoff, A. I., Singer, L. (1951) *Blood*, **6**, 413, 429.

# STRUCTURE OF RESPIRATORY TISSUE

F. D. BERTALANFFY
Ph.D. Montreal
ASSISTANT PROFESSOR OF HISTOLOGY, UNIVERSITY OF MANITOBA, WINNIPEG, MAN.

C. P. LEBLOND
M.D., D.Sc. Paris, Ph.D. Montreal
PROFESSOR OF ANATOMY, MCGILL UNIVERSITY, MONTREAL, CANADA

THE respiratory tissue of the lung consists of thin partitions—the alveolar walls—which separate the alveolar air-spaces. The alveolar walls are composed of cells, capillaries, and interstitial connective tissue. For the past hundred years there has been much controversy as to whether or not the alveolar walls are lined by epithelium. Another disputed subject has been the nature and rôle of the various types of cells present within the walls. Recently, these questions have been clarified by electron microscopy and, in our laboratory, by the use of various histochemical methods.

In this article we present evidence that a squamous epithelium lines the alveolar walls and that the cells included within these walls are connective-tissue cells. Experiments were made mostly on rats, but histochemical studies were made also on human and other mammalian lungs.

### Lining of Pulmonary Alveolar Wall

The earliest theories on the structure of the lung implied that the alveolar walls were covered by a "pavement epithelium." [1 88 51 52 107 108 37–39 45 20 21 46 24] However, descriptions of this epithelium were meagre and not supported by illustrations. Consequently they were difficult to interpret and will not be further considered here.

The first carefully worked out theory concerning the lining of the alveolar wall was based on results obtained by silver impregnation. With this technique, the surface of the alveolar walls appeared to be covered by extremely flattened structures, called "non-nucleated plates," which alternated with small nucleated cells (fig. 1).[27 25 91 105 53–55 26 71 74 48 13 14 18 47 50 34] The plates were described as thin sheets, and generally assumed to derive from the cytoplasm of flattened epithelial cells which had previously fused and lost their nuclei. How-

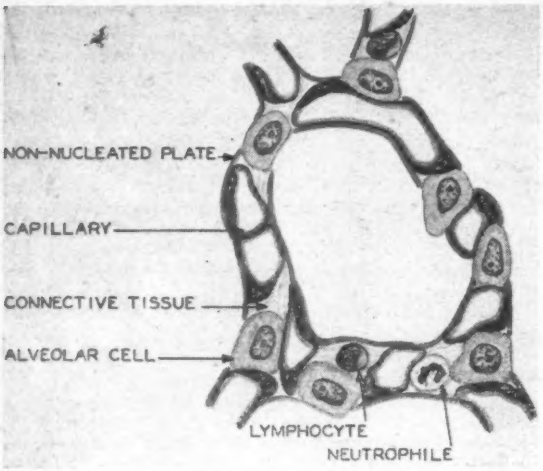



Fig. 1—" Non-nucleated plate " concept.

ever, histological methods other than silver impregnation failed to demonstrate these " non-nucleated plates " and many histologists therefore denied their existence.

These histologists developed the radical concept that the alveolar walls were not covered by an epithelial lining and that the components of the wall (capillary network, interstitial connective tissue, and cells) were exposed to the alveolar air (fig. 2).[57–59 78 79 35 93–95 103 106 16 4 5 22 68 63 98 97] In the absence of an epithelial lining, the alveoli would be a sort of physiological tissue-air space, a " functional interstitial emphysema." [68 40]

The concept of a " bare " alveolus was not accepted by a group of workers who considered the alveolar walls to be lined by a simple squamous epithelium composed of very flattened cells which may or may not form a continuous lining (fig. 3).[47 56 83 100 49 90 75 76 6 7 32 96 88] Normally almost indistinguishable with the light microscope, the epithelium was said to become visible under experimental and pathological conditions producing an œdematous exudation which raised it from the underlying tissue.[72 73]

The three main concepts of the lining of the alveolar wall—" non-nucleated plates " (fig. 1), " bare alveolus " (fig. 2), and simple squamous epithelium (fig. 3)—were none of them supported by evidence decisive enough to promote general agreement. Recently, however, modern histochemical methods and electron microscopy have supplied precise evidence in favour of the existence of a simple squamous epithelium lining the surface of the alveolar walls.

In 1951 our application of the periodic-acid Schiff technique to the rat lung revealed a thin continuous purple-staining membrane on the surface of the alveolar wall.[60] Since the membrane had the same appearance and staining properties as reticular fibres and basement membranes, it was tentatively called a " surface reticulin membrane." This membrane, which was generally a fraction of a micron thick, appeared either stretched or wavy according to the degree of expansion of the particular area of alveolar tissue. Cross-sections of alveolar walls revealed that the membrane covered both sides of each alveolar septum and extended around the club-shaped widening of their free ends. Though the membrane was for the most part continuous, short breaks were occasionally observed, where often a cell of the type described below as alveolar cell protruded into the air-space.[8] Occasionally the membrane was in contact with similarly staining membranes extending into the alveolar walls. These structures, which were tentatively referred

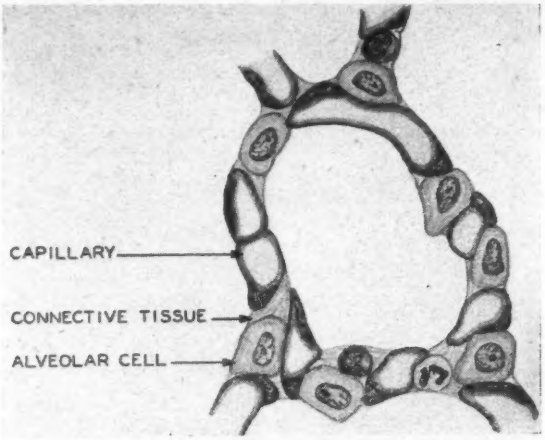



Fig. 2—" Bare alveolus " concept.

to as " internal reticulin membranes," [60] are presumed to be due to either projections of the surface reticulin membrane into the underlying tissue or to poorly distinguishable portions of capillary basement membranes. In addition, the interstices between the membranes and cellular elements appeared to be filled by amorphous material which was lightly stained with periodic-acid Schiff and may have the rôle of " cementing material " for the components of the alveolar wall.

In 1952 Low and Daniels [65] published electron-micrographs of alveolar tissue which indicated that the alveolar walls were covered by a continuous squamous epithelium composed of long flat cells with exceedingly attenuated cytoplasm. The cytoplasmic extensions were about 0·1–0·2 μ thick, and the flat nuclei were widely separated from one another. The micrographs of Low and Daniels did not show any structure corresponding to the surface reticulin membranes.

The apparently contradictory results of the two groups of investigators were reconciled by further independent work in both laboratories.

Low [66] subjected the respiratory tissue to prolonged fixation in osmic acid before electron microscopy, and thus detected a membrane underlying the pulmonary surface epithelium. He pointed out that, after prolonged fixation in osmic acid, it was difficult to preserve the fine cytoplasmic extensions of the epithelium—a result which

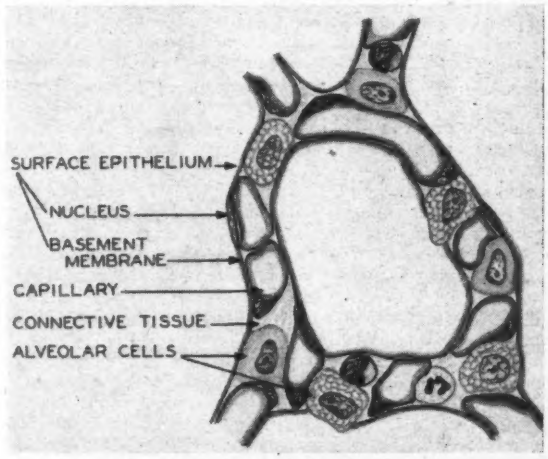



Fig. 3—" Surface epithelium " concept.

may explain why these were not seen by Swingart and Kane[103] or Policard et al.[82]

Meanwhile, using sections of human and animal lungs stained by the periodic-acid Schiff technique and counterstained with a nuclear dye, we observed flat endotheliform nuclei scattered sporadically outside the "surface reticulin membrane." Though little or no cytoplasm was visible in their vicinity, these nuclei must have belonged to cells in direct contact with the alveolar spaces.[9] Accordingly, these nuclei were thought to be part of a surface epithelium, although so little cytoplasm was observed that it was impossible to decide whether the epithelium was continuous or not. In any case, it was concluded that the surface reticulin membrane seen in periodic-acid Schiff-stained sections represented the basement membrane of this epithelium.[11] It should be noted that the frequency with which the superficial nuclei were seen in our preparations was not high, since on the average about two were found per high-power (×1200) microscopic field.

When the classical theories were re-examined in the light of these observations, it was apparent that the nuclei here described as part of the surface epithelium were considered by the supporters of the "bare alveolus theory" (fig. 2) to belong to the capillary endothelium. The "non-nucleated plates" described in the first concept (fig. 1) may be the cytoplasm of the epithelial cells, since silver impregnation may outline these cells without demonstrating their nuclei, as may be the case after impregnation of vascular endothelia. In any case, our observations as well as electron microscopy have led to the conclusion that the alveolar walls are lined by two juxtaposed structures—a squamous epithelium and its basement membrane. This conclusion supports the concept illustrated in fig. 3.

### Cells in Alveolar Walls

The capillaries present in respiratory tissue consist of a *simple squamous endothelium* supported by a basement membrane that stains with periodic-acid Schiff reagent.[60] The elongated and darkly stained nuclei of the capillary endothelium look like those of the surface epithelium, which therefore can be distinguished only by their position outside the surface membrane. Formerly we included both types of cells in the same category and referred to them collectively as "endothelium-like cells."[12] The nuclei of these cells constitute about 56% of all nuclei present in the respiratory tissue of the rat.

Since it was known that *white blood-cells* are common in respiratory tissue,[33 92] it was not surprising that leucocytes—some of which were in the lumen of the capillaries while others had migrated into the interstitial tissue—accounted for 13% of the cells present.[12]

The remainder of the cells observed in the alveolar walls (31%) constitutes a rather complex group which may show morphological differences but share several properties and are therefore grouped under the common name of "alveolar cells." (Other names for these cells are alveolar epithelial cells, septal cells, epicytes, alveolar phagocytes or macrophages, and dust cells.) By using Orth-fixed preparations stained with Masson's trichrome, two main types of alveolar cells can be readily distinguished on the basis of the presence or absence of cytoplasmic vacuoles and the staining properties of the cytoplasm.[12] The cells of the first type, vacuolated alveolar cells, are characterised by a variable number of vacuoles (fig. 3), which are surrounded by acidophil cytoplasm and in vivo are filled with lipoidal material. The cells of the other type, non-vacuolated alveolar cells, may either appear like plain and poorly limited connective-tissue cells or be differentiated into cells with clearly outlined cytoplasm which stains with the light-green component of Masson's trichrome. Transitions between the two main types of alveolar cells are often observed.

The two types of alveolar cells have in common two important properties: (1) the ability to ingest foreign particles, which explains the frequent presence of particulate matter in their cytoplasm; and (2) the ability to progress by amœboid motion, which may explain the desquamation of these cells into the alveolar spaces. The desquamated alveolar cells pass into the bronchioles, ascend bronchi and trachea, reach the pharynx, and eventually are lost in the sputum.[28 29 89 99 12 44]

The loss of alveolar cells via the respiratory passages appears to be a constant physiological phenomenon in the rat and other mammals[101 12] as well as in man.[84 62 85 67 36] It has been shown in the lung of the rat that the cellular loss is balanced by rapid mitotic proliferation[12] by which the entire stock of alveolar cells is renewed about once a week.

With a few exceptions—e.g., Osler[77]—the histologists of the last century believed that the alveolar cells were remnants of the epithelium lining the primitive cavities in the fœtal lung and were therefore epithelial in origin. The epithelial nature of the alveolar cells was also upheld by many modern histologists.[1–3 95 4 5 22 23 68–70 73 41–43]

In contrast, other workers[104 57–59 78–81 20 21 15 19 61 87 63 64] have classified alveolar cells as connective-tissue cells, owing to their behaviour (phagocytosis and amœboidism) and their morphological appearance (lack of regular epithelial arrangement, and absence of basement membrane of their own). Our histological and histochemical work supports this school of thought. Thus, toluidine-blue revealed a variable metachromatic reaction of the cytoplasm of differentiated alveolar cells—a specific property of some connective-tissue cells. Furthermore, after Masson's staining of Orth-fixed preparations, the loose connective tissue of various organs—e.g., submucosa of intestine—displayed cells like the vacuolated and non-vacuolated alveolar cells of the respiratory tissue. Within the lung itself, some of the non-vacuolated alveolar cells are indistinguishable from ordinary fibroblasts; and these show transitional forms relating them to the other types of alveolar cells. We therefore conclude that the alveolar cells belong to the large connective-tissue family, within which, owing to their phagocytic ability, amœboidism, and capacity to become pathological cells (foam cells, exudate cells, and giant cells), they may be classified as cells of the reticulo-endothelial system.

Recently, examination of lungs of toads, salamanders, and frogs has proved that the respiratory tissue of these amphibia is lined by a basement membrane that stains with periodic-acid Schiff reagent and supports a continuous surface epithelium which is more clearly visible under the light microscope than that of mammalian lungs. In addition, this epithelium overlies vacuolated and non-vacuolated alveolar cells as well as capillaries.[10] These observations suggest that the respiratory tissue has the same basic structure in mammals and amphibia.

The concept outlined here implies that the alveolar tissue is lined by epithelium composed of extremely attenuated squamous cells resting upon a basement membrane, and that the alveolar cells within the walls are connective-tissue cells at various degrees of differentiation. This concept is in line with the classical tenets of histology, since it implies that, like many other tissues, the alveolar wall displays the association of an epithelium with an underlying connective-tissue stroma.

This work was supported with grants from the National Research Council and the National Cancer Institute of Canada.

### REFERENCES

1. Addison, W. (1842) *Phil. Trans.* B. **132**, 157.
2. Aschoff, L. (1926) *Z. ges. exp. Med.* **50**, 52.
3. — (1935) *Frankfurt. Z. Path.* **48**, 449.
4. Bargmann, W. (1936a) *In* von Möllendorff, W. Handbuch der mikroscopischen Anatomie des Menschen. Berlin; vol. v, 3rd part, p. 799.
5. — (1936b) *Z. Zellforsch.* **23**, 335.
6. Bensley, R. D., Bensley, S. H. (1935) *Anat. Rec.* **64**, 41.
7. Bensley, S. H., Groff, M. B. (1935) *Ibid*, p. 27.
8. Bertalanffy, F. D. (1952) *Ibid*, **112**, 311.

9. — (1954) PH.D. thesis, McGill University.
10. — (1955) *Anat. Rec.* **121**, 265.
11. — Glegg, R. E., Eidinger, D. (1954) *Canad. med. Ass. J.* **70**, 196.
12. — Leblond, C. P. (1953) *Anat. Rec.* **115**, 515.
13. Binet, L. (1926a) *Bull. Soc. Méd. hôp. Paris*, **50**, 1319.
14. — (1926b) *Pr. med.* **34**, 931.
15. Bloom, W. (1928) *Arch. Path.* **6**, 827.
16. Brodersen, J. (1933) *Z. mikr.-anat. Forsch.* **32**, 73.
17. Buhl, L. (1874) Inflammation of the Lungs: Tuberculosis and Consumption. New York.
18. Cappell, D. F. (1929) *J. Path. Bact.* **32**, 675.
19. Chiodi, D. V. (1928) *Arch. Anat., Strasbourg*, **8**, 311.
20. Chrzonszczewsky, N. (1863) *Würzburg. med. Z.* **4**, 206.
21. — (1866) *Virchows Arch.* **35**, 165.
22. Clara, M. (1936) *Z. mikr.-anat. Forsch.* **40**, 147.
23. — (1937) *Ibid*, **41**, 321.
24. Colberg, A. (1867) *Disch. Arch. klin. Med.* **2**, 453.
25. Eberth, C. J. (1864) *Würzburg. naturwiss. Z.* **5**, 84.
26. Ebner, V. von (1899) Kölliker. A. Handbuch der Gewebelehre des Menschen. 6th revised ed., Leipzig; vol. III, 1st part, p. 304.
27. Elenz, E. (1864) *Würzburg. naturwiss. Z.* **5**, 66.
28. Engelsmann, R. (1924) *Z. klin. Med.* **100**, 315.
29. — (1926) *Z. Tuberk.* **44**, 373.
30. Fried, B. M. (1927) *Arch. Path.* **3**, 751.
31. — (1934) *Ibid*, **17**, 76.
32. Gazayerli, M. (1936) *J. Path. Bact.* **43**, 357.
33. Gerlach, W., Finkeldey, W. (1926) *Verh. dtsch. path. Ges.* **21**, 173.
34. Goyanes, J. (1936) *Sang*, **10**, 992.
35. Gross, F. (1927) *Beitr. path. Anat.* **76**, 374.
36. Gross, P. (1953) *Amer. J. clin. Path.* **23**, 116.
37. Hall, C. R. (1855a) *Brit. foreign med.-chir. Rev.* **15**, 477.
38. — (1855b) *Ibid*, **16**, 465.
39. — (1857) *Ibid*, **20**, 204.
40. Ham, A. W., Baldwin, K. W. (1941) *Anat. Rec.* **81**, 363.
41. Hayek, H. von (1948) *Klin. Wschr.* **26**, 723.
42. — (1952) *Ergebn. Anat. EntwGesch.* **34**, 144.
43. — (1953) Die menschliche Lunge. Berlin.
44. Hengstmann, H. (1953) *Z. klin. Med.* **150**, 283.
45. Hertz, H. (1863) *Virchows Arch.* **26**, 459.
46. Hirschmann, H. (1866) *Ibid*, **36**, 335.
47. Huguenin, R., Foulon, P., Delarue, J. (1929) *Ann. Anat. path. méd.-chir.* **6**, 775.
48. Jaulmes, C. (1925) *Bull. Histol. Tech. micr.* **2**, 192.
49. Jeddeloh, B. zu (1931) *Beitr. path. Anat.* **86**, 387.
50. Jeker, L. (1933) *Anat. Anz.* **77**, 65.
51. Kölliker, R. A. (1849) *Z. wiss. Zool.* **1**, 48.
52. — (1854) The Lungs. Philadelphia; p. 574.
53. — (1881a) *Verh. phys.-med. Ges. Würzburg*, **15**, 12.
54. — (1881b) *Ibid*, p. 24.
55. — (1881c) *Ibid*, **16**, 1.
56. Küttner (1876) *Virchows Arch.* **66**, 12.
57. Lang, F. J. (1925) *J. infect. Dis.* **37**, 430.
58. — (1926) *Arch. exp. Zellforsch.* **2**, 93.
59. — (1930) *Virchows Arch.* **275**, 104.
60. Leblond, C. P., Bertalanffy, F. D. (1951) *Canad. med. Ass. J.* **65**, 263.
61. Lemon, W. S., Higgins, G. M. (1932) *Amer. J. med. Sci.* **183**, 153.
62. Liebmann, E. (1926) *Schweiz. med. Wschr.* **56**, 145.
63. Loosli, C. G. (1938) *Amer. J. Anat.* **62**, 375.
64. — Adams, W. E., Thornton, T. M. jun. (1949) *Anat. Rec.* **105**, 697.
65. Low, F. N., Daniels, W. C. (1952) *Ibid*, **113**, 437.
66. — (1953) *Ibid*, **117**, 241.
67. Lundquist, J. (1932) *Uppsala LäkFören. Förh.* **38**, 1.
68. Macklin, C. C. (1936) *J. thorac. Surg.* **6**, 82.
69. — (1946) *Proc. roy. Soc. Can.* **40**, sect. v, 93.
70. — (1950) *Proc. Inst. Med. Chicago*, **18**, 78.
71. Merkel, F. (1902) *In* von Bardeleben, K. Handbuch der Anatomie des Menschen. Jena; vol. VI.
72. Miller, W. S. (1932) *In* Cowdry, E. V. Special Cytology. 2nd ed., New York; vol. I, p. 131.
73. — (1950) The Lung. 2nd ed., Springfield, Ill.
74. Ogawa, C. (1920) *Amer. J. Anat.* **27**, 333.
75. Orsós, F. (1933) *Zbl. allg. Path. path. Anat.* **57**, 81.
76. — (1936) *Beitr. klin. Tuberk.* **87**, 568.
77. Osler, W. (1876) *Can. med. surg. J.* **4**, 145.
78. Policard, A. (1926) *Bull. Histol. Tech. micr.* **3**, 236.
79. — (1929) *Pr. méd.* **37**, 1293.
80. — (1938) Le Poumon. Paris.
81. — (1947) *Bull. Histol. Tech. micr.* **24**, 127.
82. — Collet, A., Giltaire-Ralyte, L., Reuet, C. (1954) *Pr. méd.* **62**, 1775.
83. Pratt, J. H. (1900) *Johns Hopk. Hosp. Rep.* **9**, 265.
84. Propper, E. (1925) *Schweiz. med. Wschr.* **6**, 637.
85. Quensel, U. (1932) *Uppsala Läkfören. Förh.* **38**, 1.
86. Reinhardt, B. (1847) *Virchows Arch.* **1**, 20.
87. Rose, S. B. (1928) *Arch. Path.* **6**, 36.
88. Ross, I. S. (1939) *Ibid*, **27**, 478.
89. Salomon, E. (1928) *Z. Tuberk.* **50**, 65.
90. Schulha, M. (1933) *Z. Zellforsch.* **17**, 199.
91. Schulze, F. E. (1871) *In* Stricker, S. Handbuch der Lehre von den Geweben des Menschen und der Thiere. Leipzig; p. 464.
92. Seemann, G. (1927) *Beitr. path. Anat.* **78**, 526.
93. — (1929) *Ibid*, **81**, 508.
94. — (1930) *Ibid*, **83**, 705.
95. — (1931) Histobiologie der Lungenalveole. Jena.
96. Shea, S. (1936) *Proc. R. Irish Acad.* B, **43**, 73.
97. Shimai, K., Tamaru, K. (1951) *Okajimas Folia anat. jap.* **23**, 351.
98. Short, R. H. D. (1950) *Phil. Trans.* B, **235**, 35.
99. Siering, H. (1952) *Disch. Arch. klin. Med.* **199**, 443.
100. Spee, F. (1928) *Anat. Anz.* suppl. **66**, 302.
101. Stewart, F. W. (1923) *Anat. Rec.* **25**, 181.
102. Swingart, R. H., Kane, D. J. (1954) *Ibid*, **118**, 57.
103. Tschistowitsch, A. N. (1930) *Z. Zellforsch.* **11**, 333.
104. Ukawa, S. (1925) *Trans. Jap. path. Soc.* **15**, 8.
105. Veraguth, C. (1880) *Virchows Arch.* **82**, 230.
106. Wenslaw, A. (1930) *C.R. Soc. Biol. Paris*, **104**, 611.
107. Williams, T. (1855) *Med. Times, Lond.* **11**, 361.
108. — (1855) *In* Todd, R. B., The Cyclopædia of Anatomy and Physiology. London; vol. v.


# CONVULSIONS FOLLOWING PUDENDAL BLOCK BY LIGNOCAINE


W. A. W. DUTTON

M.B. Brist., M.R.C.O.G., M.M.S.A. Lond.

REGISTRAR, UNIVERSITY UNIT OF OBSTETRICS, CITY GENERAL HOSPITAL, SHEFFIELD


BECAUSE of the hazards of general anæsthesia in obstetrics (Jeffcoate 1953, Parker 1954) women who are to undergo forceps delivery frequently receive local analgesia, which is very safe and is rarely followed by toxic reactions.

## Case-report

A well-built primigravida, aged 28, was admitted to the obstetric department on March 31, 1955, on account of delay in the second stage of labour. Nothing in the history or physical examination suggested liability to convulsions. Conditions were favourable for a low-forceps delivery.

Local infiltration and bilateral pudendal block was effected with 80 ml. of 1% lignocaine ('Xylocaine') (0·8 g.) without adrenaline; no blood was aspirated, and no hæmatoma formed.

Several minutes after the injection was completed, the patient passed into coma, and an attempt to proceed with the forceps delivery precipitated a generalised clonic seizure lasting a minute. Phenobarbitone gr. 3 was given by intramuscular injection, but a second and more violent convulsion followed and continued for two to three minutes until it was controlled by sodium thiopentone 0·5 g. intravenously. The patient was cyanosed, but her colour improved after introduction of an airway and with continuous administration of oxygen. Forceps delivery was resumed and a healthy infant was born. The third stage was uncomplicated. A further gr. 3 of phenobarbitone was given by intramuscular injection. Twenty minutes after delivery, the patient again became restless and clonic movements of the limbs recommenced. A further fit was averted by intravenous injection of sodium thiopentone 0·5 g.

Thereafter, the patient made a good recovery; she was conscious and normally orientated within three hours after delivery.

## Discussion

Local analgesic drugs may produce systemic effects because of accidental intravenous injection, overdosage, deterioration of the solution into toxic breakdown products, or unusual sensitivity in the patient.

In the present case the lignocaine was injected carefully, and at most a very little can have been inadvertently injected into a blood-vessel. The maximum safe intravenous dose of lignocaine in man is uncertain. Injected intravenously in mice it is about twice as toxic as procaine (Hunter 1951). In man intravenous administration of 10 ml. of 1% procaine is well tolerated, so possibly 5 ml. of 1% lignocaine would be a safe dose. In the present case, unless the patient was unusually sensitive to the drug, it is unlikely that the convulsions were caused by accidental intravenous injection.

The maximum safe dose of lignocaine suggested by Gordh (1949) is 0·5–1 g. A larger dose is commonly tolerated but is never necessary. Carnegie and Hewer (1950) regarded 1 g. as within the limits of safety. Gordon (1955) suggested that 100 ml. of a 1% solution is the maximum safe dose for a forceps delivery. In the present case, the dose given (0·8 g.) was large, but by the usually accepted standards would not have been expected to produce a toxic reaction. But the perineum at term is highly vascular, and the absorption of injected analgesic solutions is, in my experience, greatly accelerated. Furthermore, with analgesic solutions, whereas potency increases in direct ratio to concentration, toxicity increases in geometrical ratio to concentration. It seems that in the present case the dose was unnecessarily great and the concentration too high. The manufacturers of the solution used established that it contained no toxic substances that might have caused the convulsions.

This case underlines the need for caution when substituting lignocaine, which is comparatively unproved, for procaine, which is well tried and relatively non-toxic.

Procaine is not very well diffused in the tissues, but is the least toxic of all local analgesics, and for the beginner is the drug of choice; the analgesia suffices for low-forceps delivery.

Lignocaine has many advantages over procaine. It is stable, diffuses readily, and produces rapid and profound analgesia; but it sometimes causes drowsiness, and although this effect has been regarded as an advantage (Crawford 1953) it is probably the first symptom of toxicity. Lignocaine is undoubtedly more likely than procaine to produce toxic effects. Administered subcutaneously in 0·5% solution, lignocaine has a toxicity equal to that of procaine; but in 1% solutions it is 40% more toxic, and in 2% solutions 50% more toxic (Goldberg 1949). Accordingly lignocaine should be administered as the smallest effective volume of a low-concentration solution. I have found 50 ml. of a 0·5% solution satisfactory for pudendal block.

### Summary

A case is described in which convulsions followed administration of 80 ml. of 1% solution of lignocaine (0·8 g.) for pudendal block.

For this purpose 50 ml. of a 0·5% solution of lignocaine is effective and safe.

I thank Dr. W. J. Clancy for permission to report this case, and Prof. C. Scott Russell for much help and constructive criticism.

REFERENCES

Carnegie, D. M., Hewer, A. J. H. (1950) *Lancet*, ii, 12.
Crawford, O. B. (1953) *Anesthesiology*, **14**, 278.
Goldberg, L. (1949) *Acta. physiol. scand.* **181**, I.
Gordh, T. (1949) *Anæsthesia* **4**, 4.
Gordon, J. (1955) *Brit. med. J.* ii, 489.
Hunter, A. R. (1951) *Brit. J. Anæsth.* **23**, 153.
Jeffcoate, T. N. A. (1953) *Brit. med. J.* ii, 951.
Parker, R. B. (1954) *Ibid*, ii, 65.

## LABORATORY INFECTION OF MAN WITH VIRUS OF ENZOÖTIC ABORTION OF EWES

C. F. BARWELL
M.D. Camb.
PROFESSOR OF BACTERIOLOGY, THE LONDON HOSPITAL MEDICAL COLLEGE

LABORATORY infection with psittacosis virus is a well-recognised hazard, and lymphogranuloma venereum (L.G.V.) has been acquired in similar circumstances as an infection of the upper respiratory tract (Harrop et al. 1941). The virus of enzoötic abortion of ewes (E.A.E.), which belongs to the same large group of infectious agents (Stamp et al. 1950), has not so far been recognised as a cause of human disease and, for this reason, has been regarded as probably safe to handle in the laboratory. It multiplies abundantly in the yolk-sac of the developing hen's egg, producing larger yields of virus particles than are obtained after infection with psittacosis or with L.G.V. Since it shares the heat-stable group antigen common to all viruses of this sort (Monsur and Barwell 1951), its presumed harmlessness to man has commended it for laboratory work, particularly the preparation of potent antigens for use in complement-fixation tests.

### Case-report

An Egyptian doctor, aged 35, visiting this country for postgraduate training, came to this department on Jan. 31, 1955, and worked only with E.A.E. virus in a room not used at the time for other virus studies. The work involved inoculation of eggs and the preparation of suspensions from the infected yolk-sacs. On Feb. 19 she became ill with what she believed to be "flu" but remained at work for a week and took large doses of aspirin daily. She was admitted to this hospital on Feb. 28 complaining of general malaise, headache, pain in the chest, and cough. During the weekend immediately preceding this she had had hæmaturia.

*Examination and Investigations.*—On admission her temperature was 103·4°F, pulse-rate 134, and respirations 28 a minute. Her throat was red and inflamed, and she had a persistent harsh non-productive cough. Numerous scattered crepitations were heard over the lower right chest, mainly anteriorly, and the percussion note in the right axilla was somewhat impaired. Radiography revealed pneumonic consolidation of the right middle lobe, extending into the upper part of the right lower lobe (fig. 1). A blood-count showed leucocytes 8700 per c.mm. (differential count normal) and hæmoglobin 70%. A cloud of albumin was found in a catheter specimen of urine; the deposit contained many red cells and a few granular casts. Cultures of urine and of blood were sterile.

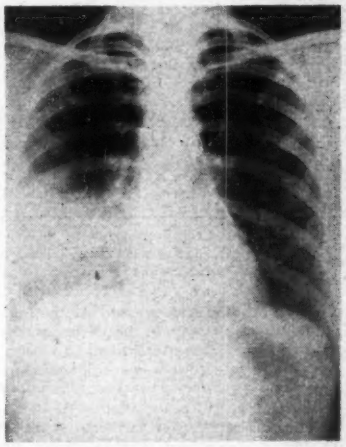


Fig. 1—Radiograph of chest on day of admission, 9 days after onset.

*Diagnosis.*—The clinical findings, notably the pronounced radiographic changes with a relative paucity of other physical signs in the chest, with the normal leucocyte-count, suggested virus or atypical pneumonia. Nothing in the history indicated that psittacosis was likely, except that the patient had, in another room, observed manipulations with that virus on a few recent occasions. Although without precedent, infection with E.A.E. virus was thought to be a possibility more in keeping with events before the illness. Sputum was produced from the day after admission and *Staphylococcus pyogenes* predominated in several cultures; at the time its presence was considered to be contributory, possibly to infection with influenza virus.

*Virus Investigations.*—Serum collected soon after admission (10 days after the onset) showed no fixation of complement when tested at 1 in 4 and higher dilutions against Q fever and heated psittacosis-virus antigens. Tests for cold agglutinins and antibodies to streptococcus M.G. were negative; these two tests and that for Q fever were again negative with serum at the 17th day of illness, but with the psittacosis-group antigen a serum dilution of 1 in 64 gave complete fixation, and to 1 in 256 partial fixation was obtained. A third specimen, collected on the 20th day, gave the same end-point, but complete fixation was found at 1 in 128. The results of these and subsequent tests are shown in table I. Since penicillin-resistant *Staph. pyogenes* was cultured from sputum received on the day after admission, and since psittacosis virus is sensitive to this antibiotic, streptomycin was added to a suspension of the specimen in broth to a final strength of 1 mg. per ml. as a preliminary to attempts to grow a virus in eggs and mice. After incubation for 2, 5, or 8 hours the material was inoculated into 4-day-old yolk-sacs. The embryos died at intervals of 4–14 days and all showed bacterial contamination of the yolk-sac, but in smears of two

TABLE I—RESULTS OF COMPLEMENT-FIXATION TESTS WITH PSITTACOSIS-GROUP ANTIGEN

| Date (1955) | Days after onset | Reciprocal of highest dilution of serum giving | |
|---|---|---|---|
| | | Complete fixation | Partial fixation |
| March 1 .. .. | 10 | Negative | Negative |
| ,, 8 .. .. | 17 | 64 | 256 |
| ,, 11 .. .. | 20 | 128 | 256 |
| April 25 .. .. | 66 | 64 | 128 |
| May 26 .. .. | 97 | 32 | 64 |
| June 2 .. .. | 104 | 32 | 128 |
| July 28 .. .. | 160 | 32 | 64 |

TABLE II—COMPLEMENT-FIXATION TEST SHOWING BEHAVIOUR OF SERUM FROM PATIENT AND FROM A KNOWN CASE OF PSITTACOSIS BEFORE AND AFTER ABSORPTION OF GROUP ANTIBODY

| Serum | Absorbed with | Dilution | Antigens | | |
|---|---|---|---|---|---|
| | | | E.A.E. virus | | Patient's virus unheated |
| | | | Heated | Unheated | |
| Patient .. | Nil | 1/16 | ++++ | ++++ | ++++ |
| | | 1/32 | ++++ | ++++ | ++++ |
| | | 1/64 | ++++ | ++++ | ++++ |
| | Heated L.G.V. virus | 1/16 | + | ++++ | ++++ |
| | | 1/32 | + | ++++ | ++++ |
| | | 1/64 | − | + | ++ |
| Known case of psittacosis | Nil | 1/8 | ++++ | ++++ | ++++ |
| | | 1/16 | ++++ | ++++ | ++++ |
| | | 1/32 | ++++ | ++++ | ++++ |
| | Heated L.G.V. virus | 1/8 | − | − | + |
| | | 1/16 | − | − | + |
| | | 1/32 | − | − | − |

Complete fixation, ++++.
Partial fixation, +++, ++ or +.
No fixation, −.

the appearances suggested that a Castaneda-positive virus was also multiplying. Successful isolation of such a virus resulted from intraperitoneal injection of the same suspension of sputum into four 6-week-old mice. No gross or microscopic abnormalities were found in two which were well when killed 5 days later, but a suspension of their spleens yielded positive results after inoculation into yolk-sacs; large amounts of virus were then seen in stained preparations, and cultures for bacteria were sterile. The virus isolated in this way differed from the psittacosis strain maintained in this laboratory in that yolk-sac passage consistently killed embryos after a longer interval (4–5 days), and the yields of virus, assessed by microscopy and antigen potency, were much larger. A more important distinction from psittacosis virus was that the two mice not killed a few days after injection of sputum did not die later of virus infection, nor was it possible to establish intraperitoneal infection in mice with the agent isolated in eggs. A few animals died but without microscopic evidence of virus growth, and further passage was without effect. Previously E.A.E. virus has been found to behave in this way, and in this instance infection of the mouse spleen, although limited, led to recovery of the agent in yolk-sac cultures with the exclusion of bacterial contaminants. This behaviour conforms with the E.A.E. laboratory strain, and confirmation of this identity was obtained by an absorption test (Bedson et al. 1949), in which sera from the patient and from a known case of psittacosis were treated with heated L.G.V. virus to remove group antibody. The results are given in table II, which shows that unheated E.A.E. virus gives specific complement fixation with the patient's serum, as does a similar antigen made from the virus isolated from her sputum; by contrast, absorption of the psittacosis serum has eliminated the reaction with these preparations. When the patient returned to work, five weeks after the start of her illness, skin tests were done with preparations of psittacosis, E.A.E., and L.G.V. viruses. Both heated suspensions of virus particles from yolk-sacs and the more specifically reactive extracts made by treatment with 0·02 *N* HCl (Barwell 1952) were injected intradermally. Two days later small papular reactions to all the heated antigens were observed; these were 4 mm. in diameter and therefore smaller than is usually taken to indicate a positive Frei test. Of the acid extracts only that from E.A.E. virus gave a reaction, and this took the form of an inconspicuous but palpable lesion 8 mm. across.

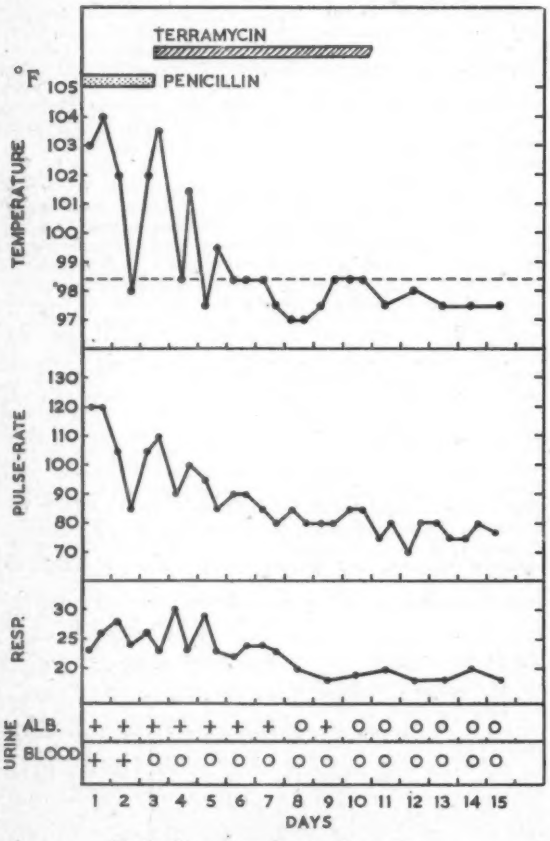



Fig. 2—Chart of treatment and progress.

*Treatment and Progress.*—From the first two days after admission penicillin 0·25 mega unit was given 12-hourly with no response. On the 3rd day a course of oxytetracycline (terramycin) was started: 0·5 g. was given 6-hourly for four doses followed by 0·5 g. b.d. for 7 days. There was rapid improvement, and the temperature was normal within 2 days (fig. 2). Progress was uninterrupted, and the patient was discharged on March 15, when radiography of the chest and examination of the urine showed no abnormalities.

Experimental infection with psittacosis in mice (Bedson and May 1945) and the disease in man can be treated with penicillin, to which E.A.E. virus is not sensitive (Dickinson and Inkley 1951). The failure of penicillin in this case is in keeping with the identity of the strain isolated from the sputum, although the course of treatment was very short and the dosage small. Terramycin is effective against E.A.E. as well as psittacosis virus.

## Discussion

The changes in the urine, first noticed a week after the onset, were taken to indicate acute focal nephritis—an unusual complication of virus infections. However, *Staph. pyogenes* was also found in the sputum and may have played a part in its development.

The large number of different psittacosis-like viruses isolated from mammals (mice, cats, sheep, cattle, and opossums) is of interest from many points of view, including man's possible susceptibility to some of them. For example, this potentiality on the part of feline-pneumonitis virus (Baker 1944) has been mentioned although not established. An infection among natives in the Belgian Congo has been attributed to another virus of the same group by Giroud and Jadin (1954), who suggest that these outbreaks may have originated from cattle, sheep, or goats. Psittacosis-group antibody was subsequently found in some of the goat sera tested by complement fixation (Giroud et al. 1954).

The case described here indicates an apparently novel activity on the part of a virus causing abortion in sheep. Since extremely large amounts of the virus may be seen in the placentæ of affected sheep, it seems possible that infection may at times take place in those tending these animals but has so far escaped recognition.

**Summary**

A case of acute virus pneumonia in a laboratory worker is reported.

The properties of the virus isolated from sputum, absorption tests on the patient's serum, and skin tests indicated that infection was due to the agent causing enzoötic abortion in ewes.

This virus had been used by the patient for experimental work during three weeks before the illness and has not previously been recorded as a cause of human disease.

I am indebted to Prof. Clifford Wilson and Dr. D. G. Abrahams for the clinical notes.

REFERENCES

Baker, J. A. (1944) *J. exp. Med.* **79**, 159.
Barwell, C. F. (1952) *Brit. J. exp. Path.* **33**, 268.
Bedson, S. P., Barwell, C. F., King, E. J., Bishop, L. W. J. (1949) *J. clin. Path.* **2**, 241.
— May, H. B. (1945) *Lancet*, ii, 394.
Dickinson, L., Inkley, G. W. (1951) *Nature, Lond.* **168**, 37.
Giroud, P., Jadin, J. (1954) *Bull. Soc. Path. exot.* **47**, 578.
— Roger, F., Dumas, N., Vouilloux, P., Sacquet, E. (1954) *Ibid.* p. 644.
Harrop, G. A., Rake, G. W., Shaffer, M. F. (1941) *Trans. Amer. climat. (clin.) Ass.* **56**, 154.
Monsur, K. A., Barwell, C. F. (1951) *Brit. J. exp. Path.* **32**, 414.
Stamp, J. T., McEwen, A. D., Watt, J. A. A., Nisbet, D. I. (1950) *Vet. Rec.* **62**, 251.

## Preliminary Communication

### THE DEMONSTRATION OF LYMPHATIC VESSELS

THE lymphatic drainage from tissues can be studied by injecting some material which will be visible in the vessels when the tissues are removed at operation or biopsy. Ideally the material injected should be (*a*) non-toxic, (*b*) diffusible on interstitial injection and readily taken into lymphatics, (*c*) rapidly removed, without causing local or general stain, when injected into living subcutaneous tissues, and (*d*) easily visible and non-diffusible in the fixed specimen.

Substances in common use do not fulfil all these criteria: thus Evans blue and patent blue tend to fade from lymphatics during mass clearing; pontamine sky-blue is more permanent, which though an advantage histologically is a disadvantage clinically; and particulate dyes tend to remain in the tissues and enter lymphatics poorly.

A new method has therefore been devised for the demonstration of lymphatic vessels in the breast. A diffusible solution containing free iron is injected into the interstitial tissues, from which it is taken up by lymphatics. When the breast has been removed, the iron is precipitated in the vessels and nodes by fixation in isotonic acid-potassium-ferrocyanide/formol saline solution, forming a permanent, particulate, and easily visible prussian blue. Various iron-containing solutions have been used, including iron dextran similar to that given by injection for iron-deficiency anæmia. A small quantity of patent blue added to the injection displays the vessels during operation, and a radio-opaque addition provides for radiographic record of the specimen.

Post mortem, injected iron can be made to enter the lymphatic vessels by massage, and its use has the advantage of avoiding extensive skin staining by dye.

Iron-containing compounds of high molecular weight, suitable for the biopsy study of superficial lymphatic vessels, are at present under investigation with Mr. David Crockett, F.R.C.S.

Middlesex Hospital, London, W.1

R. T. TURNER-WARWICK
B.M., B.Sc. Oxfd, F.R.C.S., M.R.C.P.

## Medical Societies

### HEBERDEN SOCIETY

THE annual meeting of this society was held in London on Nov. 25 and 26, under the presidency of Prof. R. E. TUNBRIDGE.

#### Spondylitis and Heart-disease

Dr. JAMES SHARP had found that of 788 patients attending a clinic for the investigation of cases of spondylitis 25 had disease of the mitral or aortic heart valves. 3 of these, all with pure aortic disease, appeared to have typical ankylosing spondylitis, and Dr. Sharp suggested that the processes in the spine and heart might be related.

In at least 7 of the remainder the changes in the heart, spine, and sacro-iliac and limb joints seemed to have resulted from severe attacks of rheumatic fever. The clinical features of these 7 and of 12 further patients, who had the same condition but had not been referred to the spondylitis clinic, were described. 17 of them had permanent change in limb-joints of the type originally described by Jaccoud, and 12 had residual limitation of spinal movement.

Radiographically the sacro-iliac joints were commonly involved. The changes in the spine were characterised by alteration in shape and sometimes hypoplasia of the vertebral bodies, narrowing and ossification of multiple discs without vertebral osteophytosis, apophyseal joint involvement progressing to bony ankylosis, and, occasionally, ossification of spinal ligaments. In its complete form this radiographic picture was recognisably different from that of typical ankylosing spondylitis.

Deep X-ray therapy did not appear to be of value for such patients, but they were usually greatly helped by aspirin. The most important measures in their long-term management were the prevention and early treatment of streptococcal infections.

#### Prednisone and Prednisolone

Dr. H. F. WEST opened a discussion on prednisone and prednisolone. The ability of prednisone to suppress the adrenal gland was approximately the same as that of a dose of hydrocortisone equal in therapeutic potency.

Dr. OSWALD SAVAGE confirmed the therapeutic effectiveness of the new substances—particularly evident in an improvement in strength of grip. In different patients they proved from two to ten times as potent as cortisone. Dyspepsia was a common toxic effect, but was not invariably worse on the new steroids than on cortisone. Afebrile pneumonia and staphylococcal septicæmia had occurred during treatment.

Dr. MALCOLM THOMPSON said that in the United States hæmorrhage from the upper or lower alimentary tract was a recognised danger of treatment with the new steroids. After several months of treatment the dose often had to be increased to maintain suppression of the disease, but a change to cortisone was sometimes an effective alternative to this.

Dr. G. D. KERSLEY had found prednisolone useful in treating a case of rheumatoid arthritis with heart-failure and œdema.

Dr. F. DUDLEY HART had been impressed by the promptness of the response to the new steroids. He felt, however, that the increased incidence of dyspepsia associated with their use outweighed the advantage of their negligible effect on sodium metabolism.

Dr. A. ST. J. DIXON commented on the "lift" which a patient experienced when he was transferred from cortisone to one of the new compounds.

Dr. E. G. L. BYWATERS stressed that the incidence of side-effects was the crux of the problem, and that it was too early to draw firm conclusions on this.

Dr. J. J. R. DUTHIE was anxious about the effect on the integrity of joints of completely suppressing inflammation and thereby removing a check to their over-use.

### Rheumatoid Arthritis in a Population Sample

Prof. J. H. KELLGREN described a survey in which a sample of the general population aged 55–64 was examined clinically, radiographically, and serologically for evidence of rheumatoid arthritis. Clinical evidence of rheumatoid arthritis was found twice as frequently in women as in men, but radiographic signs of rheumatoid arthritis and positive sheep-cell-agglutination tests were equally distributed between the sexes. In 9 out of 10 patients with severe clinical rheumatoid arthritis the diagnosis was confirmed by positive radiographic signs and/or a positive agglutination test, but with lesser degrees of clinical disease such confirmation was less usual; there were 20 patients with positive radiographic signs and/or agglutination tests among the 283 who had been recorded as free from clinical evidence of rheumatoid arthritis.

The prevalence-rates in this sample ranged from 1% for men and 3% for women for severe clinical rheumatoid arthritis, confirmed radiographically and/or by the agglutination test, to 11% for men and 27% for women where all grades of clinical disease including a past history of polyarthritis were included.

Thus precise diagnostic definition was essential for the study of comparative prevalence-rates in different populations.

### Population Study of Osteo-arthritis in Women

Dr. J. S. LAWRENCE had found radiographic osteo-arthritis in 83% of men and 87% of women in a sample of persons aged 55–64. It was multiple (more than four groups of joints affected) in 39% of men and 49% of women. Radiographically women had significantly more osteo-arthritis in the distal and proximal interphalangeal joints of the fingers, in the carpometacarpal joints, in the knees, and in the metatarsophalangeal joints of the feet. Men had significantly more osteo-arthritis in the wrists only.

Two main factors seemed to be responsible for the greater prevalence of multiple osteo-arthritis in women: (1) a factor, believed to be genetic, associated with clinical Heberden's nodes and with osteo-arthritis of the interphalangeal, metacarpophalangeal, and carpometacarpal joints of the hands, the interfacetal joints of the cervical spine, the sacro-iliac joints, and the metatarsophalangeal joints of the feet; (2) a second factor, possibly also genetic, associated with obesity and with osteo-arthritis of the weight-bearing joints only. Other causal factors —trauma, deformities, occupation, and rheumatoid arthritis—played a relatively minor rôle in determining the distribution between joints of osteo-arthritis in women.

### Arthritis and Psoriasis

Dr. V. WRIGHT described clinical and laboratory findings in 31 cases of arthritis associated with psoriasis. In 25 the arthritis was atrophic; 5 had degenerative joint disease; and 1 had rheumatic fever. Lesions in the skin most commonly antedated the arthritis; changes in the nails came on at the same time as the joint lesions much more often than psoriasis of the skin, and tended to wax and wane in parallel with the arthritis.

At its onset the arthritis was polyarticular less often than in classical rheumatoid arthritis. Although the distal interphalangeal joints were most commonly the joints first involved the process did not remain confined to them, and there seemed no reason to distinguish psoriatic arthropathy as a clinical entity in which only these joints were affected. Other clinical features of atrophic arthritis associated with psoriasis were a tendency to mimic gout, a high incidence of complete remissions, morning stiffness as a prominent symptom, and a tendency to be either very severe or very mild.

In 3 cases the picture had been of ankylosing spondylitis together with peripheral arthritis. The differential agglutination test was negative in all but 1 case—suggesting that the combination of psoriasis and arthritis was more than the coincidence of two common diseases, and that the arthritis was modified by the psoriasis if not a completely distinct entity. Among the other laboratory results, the serum-globulin level was high in 6 of 22 patients, and the serum-alkaline-phosphatase level raised in 14. Among the 5 cases with osteo-arthritis there were, rather surprisingly, 4 with changes in the nails.

### Neutral Salt-soluble Collagen

Dr. D. S. JACKSON reported a new method of isolating and purifying the so-called "alkali-soluble collagen." This involved extraction of the skins of young rabbits with neutral salt solutions followed by repeated precipitation with saturated sodium chloride or ammonium sulphate.

Physicochemical methods suggested that the particle in solution was rod-shaped, the rods aggregating to produce fibrils of 100 Å diameter having a 2000 Å spacing, which were transformed on warming to 37°C to fibres of 1000–2000 Å diameter and the typical collagen spacing of 640 Å.

### Serum-proteins in Rheumatic Fever

Dr. I. GILLILAND, Dr. I. C. ISDALE, and Dr. E. M. ABDEL-WAHAB reported their findings in an investigation of changes in the serum-proteins during an attack of rheumatic fever. The ratio of albumin to α-2-globulin (measured by paper electrophoresis) was low in the initial stages of the illness and rose steadily as the patient recovered.

## ROYAL SOCIETY OF MEDICINE

### Anæsthesia, Respiration, and Resuscitation

THE section of comparative medicine met at the Royal Veterinary College, London, on Dec. 14, under the presidency of Mr. JAMES MCCUNN, to see films and exhibits based on the theme New Apparatus and Methods of Interest in Anæsthesia, Respiration, and Resuscitation.

#### ANÆSTHESIA IN ANIMALS

Prof. C. FORMSTON showed a film of a cæsarean-section operation on a cow, using a three-rib paravertebral block; and Mr. OLIVER JONES reviewed the problem of administering an anæsthetic to a jaguar. The technique was designed to prevent any excitement stage. The animal was first placed in an airtight container and then an ether-chloroform mixture was blown in under pressure. The animal rapidly lost consciousness; subsequently it was removed from the container and endotracheal intubation was performed with a tube that somewhat resembled an outsize umbrella.

#### EXPERIMENTAL CARDIAC SURGERY

Some of the problems of cardiac surgery were underlined by two films illustrating possible experimental approaches.

Dr. A. B. COOKSON demonstrated the manner in which a dog's heart could be excluded from the general circulation for a short time with the aid of hypothermia. After being rewarmed the animal did not appear to have suffered any ill effects.

Another method was advocated by Dr. D. G. MELROSE, who outlined the principal features of the mechanical heart-lung machine. Briefly, the venous blood is withdrawn from the right side of the heart, passed through an oxygenator, and then pumped back into the aorta. With

this technique the work of the heart and lungs can be taken over while the heart or main vessels are opened under direct vision.

EXHIBITS

The exhibits included many mechanical respirators for use in anæsthesia and for patients with poliomyelitis. These machines could be divided into two main types: those that were powered by compressed air or gases, and those operated by an electric motor. It is evident that there is no general agreement on which method is the more suitable.

The majority of the respiratory machines were of the positive-pressure type: that is to say, during inspiration gases are blown into the trachea and bronchial tree under pressure, and during expiration the pressure rapidly falls to zero. Some pumps, however, were capable of exerting a negative pressure during the expiratory phase (negative-phase machines) in order to aid emptying of the alveoli. There is, as yet, no unanimity on the efficacy of the negative phase or the ideal relationship between the length of inspiration and that of expiration.

Prof. E. A. PASK showed a pump which was powered by a standard vacuum-cleaner and was capable of ventilating 6 patients simultaneously. Another feature in some of the models on show was a "patient-operated" attachment. This is particularly useful if the patient is breathing spontaneously but has insufficient muscle-power to ensure adequate ventilation. In such a case the respiratory rate can be controlled by the patient: for whereas expiration is passive, the moment inspiration starts the slightest volume change triggers-off the pump so that a full inspiratory movement is completed. Dr. J. P. PAYNE showed a positive-pressure machine which can be patient-controlled and responds to a volume change of as little as 0·5 ml. of air.

For the long-term ventilation of the patient with poliomyelitis the importance of a suitable humidifier in the inspiratory circuit was emphasised by Dr. J. M. K. SPALDING and Dr. A. CRAMPTON SMITH.

A completely different approach to the ventilation of patients with poliomyelitis was shown by Dr. J. T. SCALES and Dr. A. KINNIER WILSON, who use a British cuirass respirator. A plastic shell surrounded by thick foam-rubber at the edges is placed over the front of the patient's chest and abdomen so as to ensure an airtight seal. Inspiration is effected by sucking air out of the shell, thus pulling the ribs and abdominal wall outwards as do the respiratory muscles, and during expiration the negative pressure rapidly reverts to zero. In this way patients can be suitably ventilated in the sitting or standing position, so that the apparatus permits considerable freedom of movement and nursing care.

Among the many other exhibits was a machine for continuously following the blood-pressure, designed by Dr. J. GREEN, an apparatus for neonatal anæsthesia shown by Dr. R. W. COPE, and a phrenic-nerve stimulator which was recommended by Dr. K. W. CROSS and Dr. P. W. ROBERTS to initiate respiratory movements in the newborn child.

# Reviews of Books

## Denial of Illness

*Symbolic and Physiological Aspects.* EDWIN A. WEINSTEIN, M.D., associate neurologist, Mount Sinai Hospital, New York; ROBERT L. KAHN, PH.D., research psychiatrist at the hospital. Springfield, Ill.: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1955. Pp. 166. 34*s*.

IN the attempt to cover up something regrettable, the facts may be moulded into a plausible and unimpeachable story, and it is not long before the story-teller is convinced of its truth: that is just how it happened. In hysteria, a free-floating seed of anxiety can take root and bear a harvest of bodily discomforts and disabilities anywhere between the scalp and the toes, symptoms which do not really exist—to the other person, that is. And yet when someone has a serious disability, demonstrable to all bystanders, he can elect to deny that anything is amiss. This phenomenon of denial and unawareness of disability, termed anosognosia by Babinski, has been recognised since 1885, and various explanations have been put forward. As it was found to occur most often when blindness was associated with hemiplegia, deep-seated lesions involving the parietal lobe of the minor hemisphere and the thalamus have usually been involved—and occasionally discovered.

During the past eight years the authors of this book have been intensively investigating the changes in behaviour of 52 anosognosic patients. In addition to denial of disabilities and the necessary confabulation, nearly all of them had evidence of severe mental derangement—e.g., disorientation for time and place, paraphasia, paranoia, hypomania or depression, misidentification of persons, incontinence, and even hallucinations. Intelligence tests showed very little impairment except when the subject matter infringed on the patient's disability. Then the answers went all awry. In the person-tree-house drawing test, patients showing explicit denial can achieve symmetry, but those whose denial is only implicit will, if suffering from a left hemiplegia, omit the right side of the object in their drawing, thus mirror-imaging their disability.

Electro-encephalography revealed, in all but 1 patient, that during the period of denial there was diffuse slow wave activity on both sides, but no focal abnormality, suggesting that the relevant disruption involved the centrencephalic system. In patients whose disturbed brain function was restored, as after subarachnoid hæmorrhages, encephalitis, or the successful removal of a tumour, the slow waves disappeared, and the anosognosis was replaced by anxiety and depression or hypochondria. At necropsy, moreover, patients showed a wide variety of lesions with no one common factor.

The most interesting observation is the account of the vast improvement in orientation and social behaviour when the patients got back home, suggesting that the hospital may not always be the best place—for those who deny that they are ill, at any rate.

## Official History of the Canadian Medical Services 1939-45

*Clinical subjects*, vol. II. Editor: W. R. FEASBY, D.A., M.D., Canadian Army Medical Historian. Ottawa: Queen's Printer and Controller of Stationery. 1953. Pp. 537. $5.

DURING the late war, Canadian soldiers, sailors, and airmen served in every continent, and the results of medical experience in widely different circumstances (of environment and kinds of warfare) are clearly and comprehensively recorded in this official history. Unnecessary detail has been avoided to permit discussion of fresh topics and aspects of treatment, and an extensive statistical section provides valuable data for calculating man-power for the future. Especially useful are the chapters on burns, cardiovascular surgery, the treatment of shock, and the rehabilitation of patients with bone and joint injuries.

For those inclined to think of modern war mainly in terms of battle casualties, bullet wounds, and emergency surgery, it is salutary to be reminded of the weakening of effective man-power by the diseases regarded as largely civilian hazards. For instance, the "childish complaints"—chickenpox, measles, german measles, scarlet fever, and mumps—were by themselves responsible for 575 Canadian soldiers (equivalent to roughly one battalion) being off duty throughout the war. Gastro-intestinal disease (notably duodenal ulcer and the dysenteries) caused a high rate of invalidism, and this book estimates that "psychiatric disabilities will account for approximately 30% of all casualties invalided out of any army during war." An important innovation was made by the Canadian Army medical services and directorate of personnel selection when in 1943 they jointly introduced the PULHEEMS system of recording physical, mental, and emotional capabilities, which was afterwards adopted by the Armed Forces of many other countries, including the United Kingdom.

The companion volume (I) is devoted to the organisation of the Canadian Medical Service and descriptions of the campaigns in which it served.

## First Four Minutes

ROGER BANNISTER, C.B.E., B.M. London: Putnam. 1955. Pp. 222. 15*s*.

THE fascination of round numbers was probably one of the things that created for the four-minute mile more world-wide interest than any event in the history of

athletics. When, in 1922, the mighty Nurmi held the world record, he said he thought such a time was impossible. Nine years later, Ladoumégue, of France, was the first to beat 4–10. Runners from all over the world then chipped tenths off the record until, in 1945, Haegg, of Sweden, was within 1 4 sec. of the Everest of athletics. The question had become not will it be done, but who will do it first? And the answer, Roger Bannister, now tells his story.

Dr. Bannister says that attempts to correlate athletic ability with physical characteristics are by no means as valuable as the less scientific judgment of coaches and trainers. To his own experiments on respiration he attaches little practical value for athletes; common sense is the guide. The complete absence in the book of any reference to diet and the various traditions of old-time training is a tacit pronouncement on the systems based on superstition rather than fact. The modern view on training emphasises the education of the body by physical work and especially by "interval running."

Throughout his athletic career, indifferent to praise or censure, Bannister held and maintained certain unorthodox opinions: he considered that a course of training should be adjusted "to the energy," to ensure "a physical overdraft from greater will-power," and he maintained that physically and mentally the athlete may reach a peak perhaps only once a season, a view shared by his great predecessor, Jack Lovelock, but by few other athletes. Bannister did not compete in the 1948 Olympic Games because he felt that such an effort early in his career would prejudice his chances for 1952. He "did not expect people to understand his scheme of training." The periods of inactivity with relatively little exercise may have been the best for his particular need; alternatively, his method of training may have failed to give him the toughness he needed for an Olympic 1500 metres. He had "built himself up for one supreme explosive effort at Helsinki." Unexpectedly, he was called on to run on three consecutive days, and that may have been fatal to his plans.

However that may be, his victories last year at Berne and Vancouver were a triumphant vindication of his attitude towards training. His book shows uncommon literary ability; and quite apart from its interest to the sportsman, it gives a striking picture of a sensitive young man who has had the remarkable experience of being one of the best-known men in the world.

### Kolpofotogramme

Vol. III. *Zur Pathogenese des Portiokarzinoms und Erleichterung seiner Frühdiagnose durch farbige Kolpofotogramme.* ROBERT GANSE, DR. MED, Direktor, Frauenklinik Friedrichstadt der medizinischen Akademie Carl Gustav Carus, Dresden. Berlin: Akademie-Verlag. 1955. Pp. 120. DM. 38.

Dr. Ganse continues his study of the earliest phases in the development of carcinoma of the ectocervix. Colpophotography not only brings into view the whole thickness of the epithelium but includes the stroma and blood-vessels. The method is superior to cytological examination, and except in true erosion, leucoplakia, and early carcinoma, biopsy may be avoided. As in previous volumes, the photomicrographs are of indifferent quality, but the clarity and colour of the reproductions are quite startling.

### Collected Papers of Otto Fenichel

2nd series. Editors: HANNA FENICHEL and DAVID RAPAPORT. London: Routledge & Kegan Paul. 1955. Pp. 374. 35*s*.

THIS volume includes the papers and addresses written during the last ten years of Dr. Fenichel's life.

There is no single thread running through them, though in many of them the importance of ego-psychology is emphasised, and the social factor in the causation of neuroses is given more weight than by most English psycho-analysts. An interesting theme, insufficiently developed, is the supposedly changing form of the neuroses: Fenichel believed that in Freud's day neuroses appeared in people of intact personality, disturbed at certain points by inappropriate actions, impulses, and thoughts, whereas the "modern neurotic" has a "torn or deformed" personality which is "so involved in the illness that one cannot say at what point health ends and illness begins." He attributed this phenomenon, tentatively, to a change in morality in European and American cultures: the evidence for the supposed fact, and the explanation, deserve more inquiry.

The papers testify to Fenichel's justifiably authoritative tone during these years, his wide experience in psycho-analysis, his occasional bigotry (for example, if a young doctor while learning to be a psycho-analyst practises non-analytic psychotherapy only, "this is frank quackery"), and his boldness in speculation.

### Bickham-Callander's Surgery of the Alimentary Tract

Vol. I, II, and III. RICHARD T. SHACKELFORD, M.D., assistant professor of surgery, Johns Hopkins University School of Medicine; assisted by HAMMOND J. DUGAN, M.D., assistant in surgery, Johns Hopkins University School of Medicine. Philadelphia and London: W. B. Saunders. 1955. Pp. 2575. £21.

THIS comprehensive encyclopædia of operative surgery of the alimentary tract is concerned with techniques —operation, manipulation, endoscopy, and intubation. It is well printed and the illustrations are good. A splendid book for a library, but too expensive for most private shelves.

---

**The Subnormal Mind** (3rd ed. London: Oxford University Press. 1955. Pp. 391. 20*s*.).—These are the Heath Clark lectures delivered by Sir Cyril Burt, D.SC., in 1933. In the preface with which he introduced them to readers two years later, he pointed out that the time had now come for psychology to play a larger and more helpful part in the training of medical students and in the daily work of consultants, medical officers of health, and indeed of doctors generally. His own contributions to psychology, and especially to the study of mental subnormality in children, have demonstrated how much medicine can gain from the labours of psychologists, but it is questionable whether the lesson has been well learnt. Perhaps there has been too much semantic confusion between the discipline of psychology, applied to medical problems in the way which this book exemplifies, and, on the other hand, the medical psychology which is so closely linked to psychotherapy and so preoccupied with dynamic abstractions. In the preface to the new edition, Sir Cyril reinforces his original argument. He deplores any mechanistic conception of mental illness, and he insists that human personality has a definite hierarchical structure. The lectures themselves provide a clear and consistent account of the author's point of view regarding mentally defective, backward, delinquent, and neurotic young people. They exhibit his characteristic penchant for footnotes and tantalising references to earlier writings that are in fact regrettably inaccessible; they illustrate too his masterly capacity to present psychological material as though it were familiar, easy, and assured.

**Proctologic Anatomy** (2nd ed. Baltimore: Williams & Wilkins. London: Baillière, Tindall, & Cox. 1955. Pp. 310. 61*s*. 6*d*.).—This work by Prof. R. V. Gorsch, of New York, was first written to fill a gap left by the teaching of anatomy in American medical schools, and to present the detailed anatomy of the pelvis, colon, rectum, and anal canal, and thus meet postgraduate needs. These aims have been achieved, though the account of anal musculature is already out of date. Illustrations are many and most are good; but certain photographs of anatomical dissections are not very helpful. Surgical implications are touched upon and this aspect could usefully be expanded; for example, an analysis of the circumstances giving rise to rectal procidentia would be an advantage.

**Refresher Course for Practitioners** (Vol. I. Calcutta: Indian Medical Association. 1955. Pp. 364. Rs. 8.)—Articles appearing in the *Journal of the Indian Medical Association* between October, 1954, and May, 1955, have been incorporated in this book, which should prove as useful to Indian general practitioners as the *British Medical Journal's* refresher course is to their British colleagues.

**The Interpretation of Dreams** (London: Allen & Unwin. 1955. Pp. 692. 21*s*.).—This new translation by James Strachey of Freud's masterpiece is a reprint of that published in volumes IV and V of the standard edition of Freud's works (see *Lancet*, 1954, i, 445).

THE LANCET
*LONDON: SATURDAY, DEC. 31, 1955*

## Blood-transfusion

THE regional blood-transfusion services in this country now send out something like three-quarters of a million bottles of blood annually. More than one bottle is used for most transfusions, but even so the number of blood-transfusions now given is staggering. The transfusion services label each bottle with the ABO group and say whether the blood is Rh(D) positive or negative; the accuracy of this labelling is taken for granted, and it is a tribute to the care exercised in transfusion-service laboratories that errors are almost unknown. Hospital staffs are responsible for determining the blood-group of the patient in need of transfusion, and for cross-matching the recipient's serum with the donor cells; and it is at this stage that most difficulties arise, most variations of technique exist, and most mistakes are made. Considering the huge number of transfusions given, errors are remarkably rare. But, whereas the hundreds of thousands of safe transfusions pass unnoticed, those that go wrong cause great anxiety, and the very few that result in the death of a patient receive the full blast of publicity in the coroner's court—and elsewhere when claims for damages are made. DISCOMBE [1] says that every transfusionist, however able, may one day be a witness at an inquest; he must be prepared to explain his actions in non-technical language, and "if not a natural orator, he could with advantage practise elocution so that he can be heard in all parts of a small auditorium." This view may seem unnecessarily gloomy, but certainly only constant vigilance prevents accidents.

LOUTIT [2] has recently reviewed the causes of death and disease from blood-transfusion. The first one he lists is ignorance—ignorance, that is, of all the factors that count in safe transfusion. Up to 1900, when LANDSTEINER laid the foundations of knowledge of blood-groups, transfusions could not be given because of this ignorance; and even now, when large books describe all the blood-group systems that are known, the occasional "new" antibody appears and causes reactions. Secondly, there are technical errors—errors of grouping and cross-matching; LOUTIT points out that about 10% of mismatched transfusions result in kidney failure and death of the recipient, though methods of dealing with this accident have been much improved. The third cause is clerical error in recording the results of the tests applied. Fourthly, there are what he calls "administrative errors": donor and recipient have been correctly grouped and cross-matched and the results have been accurately recorded, but things go wrong. (As an example, he cites the disaster in which two patients in a ward had the same surname and the bloods were interchanged between the laboratory and the ward.) Finally, there are errors of judgment—giving blood to patients who are not in a fit state to receive it, or giving it too quickly, or transfusing unnecessarily so that, for example, a surgeon may operate on his day, instead of treating the anæmia with iron and operating later. The responsibility for these errors of judgment lies with the clinician in charge, and they are becoming steadily less frequent as clinicians become more familiar with the proper use of the transfusion which is so readily available. It is the mismatched transfusion that has received most publicity and the effect has been to make pathologists particularly careful about cross-matching and juniors unwilling to take the responsibility of deciding when a cross-matching is safe. A compromise has to be made: ideally, the 9 more important groups should be determined for each recipient's blood, and the blood for transfusion should show the same combination of 9 groups—but by then the patient might well be dead. At the other extreme, there is the practice of taking Rh-negative blood of the appropriate ABO group and carrying out a quick cross-matching test on a tile; but this is very wasteful of the 15% of Rh-negative donors and will miss any unusual incompatibility, especially in patients who have to have many transfusions.

To help the new houseman to choose a practical and reasonably safe transfusion technique and to understand the laboratory requirements in time and material, Dr. GEORGE DISCOMBE [1] has written a very useful, informative, and suitably dogmatic pamphlet. He points out that cross-matching and grouping errors are not always responsible for transfusion accidents, and of a series of 14 such accidents, which he had previously reviewed,[3] only 3 were due solely to laboratory errors. (DISCOMBE adds to LOUTIT's list of causes that of the worrying clinician, who wants blood within minutes.) Rarer causes of reactions are the presence of the A subgroups which give weaker reactions with anti-A sera and are so missed; the use of blood that has been stored *after* removal of the bottle cap and possible contamination; and the use of concentrated red-cell suspensions that have been prepared more than twenty-four hours before administration. He points out also that blood from a properly controlled refrigerator at 4°C does *not* need to be warmed before transfusing, unless the recipient's serum contains cold agglutinins of high titre; warming above 37°C can easily damage the blood irreversibly, and transfusion of such blood may be fatal. For cross-matching, DISCOMBE recomends a tube technique, using bovine albumin, which takes two hours before the result can be safely read; it is useful, he suggests, to set up a duplicate using saline only instead of albumin, since this detects more effectively anti-M, anti-N, anti-P, and anti-H. If expert laboratory help is available, the Coombs anti-globulin test should be performed, because this will disclose antibodies not

1. Blood Transfusion: a Guide to the Practice of Transfusion in Hospitals. By Dr. GEORGE DISCOMBE. London: Heinemann Medical Books. 1955. Pp. 54. 6s.
2. Loutit, J. F. *Med.-leg. J., Lond.* 1955, 23, 85.
3. Discombe, G. *Lancet*, 1954, ii, 936.

detectable in any other way; this test takes at least one hour and is better for being left for two hours.

DISCOMBE then takes the view that it is unreasonable to expect properly cross-matched blood for transfusion to be provided in under two hours from the arrival of the specimens in the laboratory. He reminds clinicians that when the patient is in a state of severe collapse, and it does not seem that he can wait two hours, the reason is lack of blood *volume* rather than lack of blood-cells. Consequently transfusion with one of the plasma substitutes, dextran or polyvinylpyrrolidone, should tide the patient over the waiting period. It is clear that, armed with DISCOMBE's pamphlet, the not-too-experienced resident can take a stand when faced with clinical pressure; but when a full laboratory service is to hand, the time between the request for blood and its supply can be shortened. DUNSFORD and BOWLEY,[4] in their comprehensive monograph, use much the same routine as DISCOMBE for cross-matching; they carry out saline and albumin compatibility tests and a Coombs compatibility test, and they agree that this takes two hours or so, since this is the optimum time for incubation of the test mixtures in the saline and albumin tests. The full techniques *must* be carried out for a group of "dangerous recipients"—i.e., all those who have a history of previous blood-transfusion, parous women with an obstetric history suggestive of hæmolytic disease of the newborn, and patients who have any form of hæmolytic disease. Patients who have not previously been transfused and parous women with normal children are classed as "safer recipients"; for this group DUNSFORD and BOWLEY prefer to carry out the full test schedule; but, if time presses, and if an *experienced* operator is at hand, they are prepared [5] to do a slide compatibility test with albumin and a rapid Coombs compatibility test, both of which can be read in about thirty minutes. In Denmark a rapid method of blood-grouping has been devised by ELDON.[6] In this method cards are prepared coated with a film of 'Cellophane' on which are dried samples of anti-A, anti-B, and anti-D sera and an inert control serum, each on a separate panel. The sera, which are chosen for high avidity, are mixed with sodium chloride, heparin, and dextran before drying and it is claimed that these additives prevent rouleaux formation, give large clot-free masses when agglutinated, and enable the grouping to be carried out satisfactorily at room-temperature. For testing, the dried sera are dissolved in water and then a drop of the patient's capillary blood is added to each panel and stirred. The results can be read in three minutes, and any agglutination with the inert serum indicates that the test is inadequate for that patient's blood. It is perhaps possible that such a technique can be adapted to cross-matching, and ZEITLIN [7] suggested a method for obstetric emergency transfusions, but he used only Rh-negative blood. ELDON states that 6 out of 15,000 grouping tests were found to be incorrect. Unfortunately an error of 4 per 1000 cannot be disregarded when blood-grouping is involved, because at least 250,000 transfusions annually are given in this country; but the method may be developed further. More reliable methods of accelerated Rh-typing have been proposed by STRATTON [8] and HARVEY.[9]

In an uncompromising comment on the present situation, Dr. ALISTAIR FRENCH, secretary of the Medical Protection Society, has said [10] that junior residents should not be called upon to perform cross-matching tests, and that if necessary "the pathologist must be got out of bed to perform this heavy and responsible task." We wonder what he would say to the practice, which some hospitals have to adopt, of sending for a technician to perform this work after hours. The answer seems to lie in the classification of "dangerous" and "safer" recipients which we have mentioned. Hospitals that have no resident clinical pathologist should not undertake work in which transfusion is often needed—for example, thoracic surgery, or the care of patients with blood-diseases that need repeated transfusion. If a "dangerous" recipient is admitted in urgent circumstances then the pathologist, and no-one less, must be called, but when safer recipients are to be transfused then, if DISCOMBE's techniques are followed, the normal resident staff should be able to tide over the immediate emergency.

## Pulmonary Embolism

As we observed a year ago,[11] pulmonary embolism is commoner than was formerly supposed, and in the old and feeble it may appear so quietly as to be overlooked. It is hard to say just how common emboli of this kind are; but the incidence of massive postoperative emboli may be more readily estimated. In an assessment of fatal postoperative pulmonary embolism from many centres, both in the United States and elsewhere, DE BAKEY [12] gives an incidence of 14 per 1000 operations; but the figures from hospital to hospital and from year to year in a particular hospital vary bewilderingly. Many of these statistics may be misleading because they pay little attention to the degree of care in the post-mortem search for the embolism and primary venous thrombosis, or to the criteria used in clinical diagnosis. Certain conclusions, however, are accepted by most authorities. There is, for example, a general feeling that the incidence of pulmonary embolism in any hospital population rises and falls over the years. If true, this makes it very hard to assess prophylactic measures, because succeeding years cannot be strictly comparable. Another view with much to support it is that pulmonary embolism is as common in medical as in surgical wards. There is no definite sex predominance; and although embolism has been recorded at the extremes of age, it is commonest between 40 and 60. Beyond these few facts, strikingly little can be derived with certainty from vital statistics.

The thrombosis responsible for pulmonary infarction is usually in the leg,[13] and there are many conditions which predispose to its formation. BYRNE [14] found that cardiac disease was the most significant factor associated with the combination of venous thrombosis and pulmonary embolism in a general hospital population; it was present in 28% of his series of 748 patients.

4. Dunsford, I., Bowley, C. C. Techniques in Blood Grouping. Edinburgh, 1955.
5. Dunsford, I., Bowley, C. C. *Ibid*, p. 179.
6. Eldon, K. *Dan. med. Bull.* 1955, **2**, 33.
7. Zeitlin, R. A. *Lancet*, 1954, i, 23.
8. Stratton, F. *Brit. med. J.* 1955, i, 201.
9. Harvey, P. W. *Ibid*, p. 203.
10. French, A. *Med.-leg. J., Lond.* 1955, **23**, 85.
11. *Lancet*, 1955, i, 34.
12. De Bakey, M. E. *Int. Abstr. Surg.* 1954, **98**, 1.
13. Bauer, G. *Acta radiol., Stockh.* 1945, **26**, 511.
14. Byrne, J. J. *New Engl. J. Med.* 1955, **253**, 579.

This is compatible with previous investigations, though the corresponding figures for associated heart-disease have varied from 13% to 80%. If only fatal pulmonary emboli were considered, then heart-disease was present in 73% of BYRNE's cases. About a quarter of the emboli in this series followed an operation; and an operation for a malignant lesion seemed especially liable to be followed by infarction. The association of carcinoma with spontaneous superficial and deep phlebitis and sometimes pulmonary embolism is, of course, well recognised, and was described by TROUSSEAU in his patients and himself almost a hundred years ago. Carcinoma of the pancreas may be the one most often associated with Trousseau's sign, although in BYRNE's postoperative patients cancer of the colon was the chief culprit. Other conditions associated with postoperative embolism are venous stasis due to bed rest, dehydration, shallow pulmonary ventilation, trauma to the venous intima, and changes in coagulability of the blood. Platelet stickiness, rise in fibrinogen level, and shortened coagulation time are among the blood defects recognised. 6% of BYRNE's cases were associated with infection, 5% with pre-existing varicose veins, 5% with childbirth, and 5% with hemiplegia. BYRNE has reviewed only those patients in whom the pulmonary infarction was associated with clinical signs of venous thrombosis in the calf. But it is common experience (for the physician as well as the surgeon) that most lethal emboli strike with dramatic suddenness, bringing vicious chest pain and hæmoptysis before any diagnosis of limb thrombosis has been made.[15] Death may sometimes be heralded by premonitory emboli, but usually it is the first episode that is (almost instantaneously) fatal.[16]

The foremost problem is prevention, and there is little progress to record. The popularity of early postoperative ambulation has waxed and waned. DE BAKEY concludes that those institutions which have faithfully pursued early postoperative ambulation have proved no decrease in the incidence of pulmonary embolism; indeed, in many there has been an increase. But FARQUHARSON[17] holds that really *early* ambulation does prevent thrombosis. There is a growing conviction that prophylactic division of the femoral veins is unjustified, although the method is still much used, especially in the United States, in elderly patients and those prone to thrombosis. We cannot with certainty prevent emboli, and it is no easier to detect the thrombosis before the clot fragments. Tests for this purpose have been designed from time to time, but none has been satisfactory. Even when it comes to the management of a patient in whom an embolism is suspected, there is no general agreement. The Swedish workers, led by JORPES[18] and BAUER,[19] have made a good case for anticoagulants. Femoral or more proximal venous ligation has equally enthusiastic supporters, including BYRNE. Others believe that, as it is the first embolism that kills, if the patient survives he has little to fear from later ones. There is statistical evidence for this view, but at present most people will be prepared to disregard it and use anticoagulants when there is a threat of phlebitis, phlebothrombosis, or embolism.

15. Marks, J., Truscott, B. M., Withycombe, J. F. R. *Lancet*, 1954, ii, 787.
16. Paaby, H. *Acta chir. scand.* 1955, **109**, 319.
17. Farquharson, E. L. *Lancet*, Sept. 10, 1955, p. 517.
18. Jorpes, J. E. Heparin in the Treatment of Thrombosis. London, 1940.
19. Bauer, G. *Lancet*, 1946, i, 448.

# Annotations

## TUBERCULOSIS AND LIVER BIOPSY

HÆMATOGENOUS dissemination of tubercle bacilli is regarded as a rare complication of localised tuberculosis, except in the early post-primary period and in the terminal stages of the disease. Certainly, attempts to cultivate the organisms from the blood-stream at any stage of the disease fail with very few exceptions. But the findings of Haex and Van Beek,[1] who performed aspiration liver biopsies on 189 proven cases of tuberculosis and 150 controls, suggest that, despite the negative blood-cultures, dissemination via the blood-stream is a frequent, and perhaps almost invariable, accompaniment of the localised disease. Objective evidence of dissemination, revealed as submiliary tubercles in the biopsy specimen, was found in almost every form of tuberculosis, including primary infection, "typho-bacillosis," pleurisy, pericarditis, peritonitis, and lymphadenitis, as well as in cases involving the lungs, kidneys, adrenals, eyes, bones, and joints. Positive results were also obtained in 14 out of 20 cases of erythema nodosum and, still more surprisingly, in each of 4 cases of erythema induratum (Bazin's disease). Haex and Van Beek emphasise that the remarkably high proportion of positive results in their series was obtained only by meticulous search of every one of the hundred or so serial sections into which each biopsy specimen was cut.

In many patients the evolution of the disease was followed by repeated biopsies. For this purpose the hepatic lesions were classified according to their location, size, presence or absence of caseation or fibrinous exudate, the type of cellular exudate, and the presence and type of giant-cells. Acid-fast bacilli could almost always be demonstrated in lesions undergoing caseation, but rarely in non-caseating tubercles. Only 4 out of 70 guineapig inoculations proved positive. The age of the lesion was assessed by the proportions of epithelioid-cells, fibroblasts, fibrocytes, and scar tissue with or without hyalinisation. In many patients there was evidence of hæmatogenous dissemination continuing for several months despite what is usually regarded as adequate treatment with streptomycin and *p*-aminosalicylic acid. A similar study of 563 liver biopsies in tuberculous patients recently reported by Oldershausen et al.[2] only partly confirms the findings of Haex and Van Beek. In this investigation miliary tubercles, or what the authors term "retothelial nodules," were found in 193 specimens—an incidence of about 34%. In the 384 patients with "non-hæmatogenous" pulmonary tuberculosis the incidence was 26·5%.

This rather striking difference in the results of the two investigations may, at least in part, be accounted for by differences in technique and the thoroughness with which the specimens were searched. The matter is obviously of considerable importance not only in the diagnosis and treatment of tuberculosis but in the effect it may have on our views about pathogenesis.

## OLD PEOPLE'S REAL NEEDS

UNTIL 1948 institutional care of those in need was provided by the local authority, generally in public-assistance institutions. Most of these were built in the middle of the 19th century to cope with vagrancy and destitution, which had greatly increased after the Industrial Revolution. Grey and cheerless, with narrow dormitories approached by steep stone staircases, they reflected the austerity of the Early Victorian approach to the problems of social inadequacy.

1. Haex, A. J. C., Van Beek, C. Tuberculosis and Aspiration Liver Biopsy: Its Clinical Significance in Diagnosis and Therapy. Haarlem: Erven F. Bohn. 1955. Pp. 106.
2. Oldershausen, H. F. V., Oldershausen, R. V., Tellerz, A. *Klin. Wschr.* 1955, **33**, 104.

In time the need for this kind of accommodation was largely limited to the aged and infirm and to a few chronic sick in the younger groups. Wards as well as dormitories were required for these residents, and many local authorities used the powers conferred on them to build modern hospital units or to adapt the old institutions. Thus, when the National Health Service was started in 1948, most institutions included hospital accommodation, varying widely in comfort and efficiency, as well as the "House," or residential section, where people with social rather than medical needs were admitted.

By the National Health Service Act of 1946 responsibility for those in need of hospital care was given to the regional hospital board, while the welfare work carried on in the same institution was left under the local authority. To cope with this administrative problem, a joint-user arrangement was brought into force, and the authority owning and controlling the institution—generally the regional hospital board—continued to provide accommodation for those who were the responsibility of the other authority. When the hospital accommodation of the old institutions was thus drawn into the main hospital service many of the defects due to its historical development were put right. In many areas wards were reconstructed and redecorated; treatment centres equipped with facilities for investigation and treatment were set up; and a more enlightened approach to the disabilities of old age was introduced. Nevertheless much still remains to be done. The obvious need for home-like living quarters has stimulated some local authorities to provide separate small hostels for old people outside the institutions, but many are still accommodated in the residential sections of the old institutions. Though in some places attempts have been made to improve this accommodation, in others conditions remain substantially the same as they have been for many years. Modernisation of the buildings is expensive, and if the institution is under the regional hospital board improvement of the residential part has to compete with other hospital needs.

A report [1] on these institutions, made lately by a working party of West Cornwall Hospital Management Committee, remarks on the vivid contrasts between the listless degenerating residents in the jointly used institutions and the bright vivacity shown by those in the County Council's Old People's Homes. "Those in jointly-used institutions are for the most part content to sit thoughtless, despondent, and inactive all day long, the only interruption to their monotony being mealtimes. In the Old People's Homes there is an active interest in life, the residents get out and take part in the life of the community, join local libraries and are obviously very much alive." So sharp was the contrast between these two groups of old people that the working party at first thought that it must be due to selection of those sent to the hostels. But during their survey at one institution, where the old people lived and had their meals with low-grade imbeciles, the working party found one old man "who was still alert, intelligent and self-respecting" and discovered that he was the last person to be admitted. They began to wonder whether in such an atmosphere it would not take "a man of unusual stamina to hold on to a decent standard of life"; and by the end of their survey, which included visits to institutions where the accommodation was "worse than is usual in common lodging-houses," they had decided that it is not "surprising that there is rapid deterioration after admission to such places." This survey shows that, in one part of the country at any rate, the situation is not nearly so satisfactory as Miss Hornsby-Smith makes out in a parliamentary answer reported on a later page.

1. *Western Morning News*, June 29, 1955.

Clearly the accommodation in institutions should be largely replaced by further small residential homes; but in planning these it should be borne in mind that a main object of our welfare services for elderly people should be to enable them to remain comfortably at home in their familiar surroundings and near their friends. The hostel, however well run, cannot be a complete substitute for home, and it should be reserved mainly for infirm old people who require more care and attention than can be given them at home. Yet many of the smaller hostels opened in recent years, excellent though they are in many ways, only accept residents who can, for instance, go upstairs unaided and attend to their personal needs. In planning future hostels the needs of the frail or infirm old person should be met by providing more ground-floor bedrooms and dormitories or by installing lifts. More staff will also be needed to help them during the night, and to nurse them in short illnesses. Hostels for frail old people may be more difficult and expensive to run; but, as so often, it is the difficult and expensive that is needed and that may prove the easiest and the cheapest in the long run.

## T.S.H. AND EXOPHTHALMOS

THE idea that the thyroid-stimulating hormone (T.S.H.) produced by the anterior pituitary might be the cause both of thyrotoxicosis and of the exophthalmos which often accompanies it has been under discussion for the past twenty years or so. It still remains no more than a suggestion which, after much hard work in many quarters, has not yet been either dismissed or finally proved. The latest work on the subject was described at a recent meeting of the section of endocrinology of the Royal Society of Medicine by Prof. A. Querido, of Leiden, and Dr. I. Gilliland. Each had developed his own method of estimating T.S.H. in the blood. Professor Querido used the rate of uptake of $I^{131}$ by the mouse thyroid as an index of T.S.H. activity, while Dr. Gilliland used the rate of decay of thyroid radioactivity in chicks which had already received a loading dose of $I^{131}$. The two methods seemed to have about the same degree of sensitivity and reliability, and the results obtained were remarkably similar. The amount of T.S.H. in the blood of normal persons is only just detectable in most cases, and in some none may be found. Patients with myxœdema from any cause (except pituitary failure) nearly always have an increased T.S.H. level in the blood. Dr. Gilliland had, however, seen a few cases of extreme myxœdema without detectable circulating T.S.H. He explained these by suggesting that in prolonged severe hypothyroidism the pituitary is itself affected and can no longer make T.S.H. This view was strongly supported by the finding, in one of Dr. Gilliland's cases, that T.S.H. was originally absent but after brief and partial treatment of the myxœdema it appeared in the blood in quite large quantities.

In patients with thyrotoxicosis, but without exophthalmos or other eye signs, the level of circulating T.S.H. is no greater than normal. It may also be normal in some cases with well-developed eye signs, but in others there may be extremely high values. Both speakers at the Royal Society of Medicine agreed that there was a general tendency for exophthalmos to be associated with high levels of circulating T.S.H., but when studied in detail the correlation often broke down. In particular, Professor Querido was much impressed by a single case, in which the exophthalmic ophthalmoplegia syndrome progressed rapidly, in spite of a low level of T.S.H. in the blood.

The mere fact that patients with myxœdema have much T.S.H. in their blood, but no exophthalmos, is enough to disprove the simplest answer to the problem. It seems clear that a complex situation exists which can

only be unravelled by the development of new techniques. An obvious question to ask (but which cannot at present be answered) is whether the substance in the blood of patients with myxœdema is the same as that in the blood of patients with exophthalmos. Or is there something else in the patients with exophthalmos which makes them sensitive to the action of T.S.H.? Possibly T.S.H. is irrelevant altogether, for Dobyns et al.[1 2] claim that the pituitary makes a quite separate hormone which produces exophthalmos in the Atlantic minnow and can be found in the blood of patients with exophthalmos. It seems highly probable that the pituitary has something to do with the production of exophthalmos but both the nature of the connection and the other factors involved remain obscure. A recent report from Paris,[3] describing the beneficial effect of hypophysectomy in a case of rapidly progressing exophthalmos supports this view.

## SCREENING TESTS FOR ARGENTAFFINOMA

THE discovery of the endocrine activities of argentaffinomata is being rapidly exploited. The syndrome of flushing, pulmonary stenosis, and diarrhœa has now been described in a substantial number of cases, and its relation to the secretion of 5-hydroxytryptamine (5-H.T., serotonin, enteramine) by the tumour is now well established.[4 5] Because 5-H.T. is rapidly oxidised to 5-hydroxy-indole acetic acid (5-H.I.A.A.) in its passage through the lungs,[6] estimation of the original hormone in blood or urine is unreliable as well as difficult; and it is now generally recognised that estimation of 5-H.I.A.A. in the urine, in which it appears in large amounts in these cases, is the best diagnostic method.

Earlier methods for the estimation of 5-H.I.A.A. were necessarily fairly cumbersome, involving relatively tedious extraction or paper chromatography. To realise the potential value of the method in diagnosis (in, for example, obscure instances of cyanosis, hepatomegaly, pulmonary-valve disease, or subacute small-bowel obstruction), simpler methods were clearly needed. In a leading article last month,[5] we suggested that "it should not be outside the bounds of possibility to devise a qualitative method suitable for use in the clinical side-room." We based this observation only on the known reactivity of 5-H.I.A.A. and the large amounts excreted (as much as a gramme daily). In fact, a method which almost fulfils this criterion was published in September by Szoerdsma, Weissbach, and Udenfriend.[7] Their method, however, is less simple than the one described on p. 1359 of this issue by Mr. Hanson and Dr. Serin. They have abandoned the 1-nitroso-2-naphthol reaction of most recent authors and reverted to Ehrlich's aldehyde reagent, originally recommended by Erspamer and Borelli. They describe two methods: (*a*) a quantitative method, involving simple ether extractions and photometric estimation; and (*b*) a qualitative method, involving mere mixing of equal quantities of reagent and urine in a test-tube and boiling. The first is one of several similar methods now becoming available, and only use and direct comparison will show which is most satisfactory in practice. It is of interest, however, that Dr. Curzon, whose paper also appears on an earlier page, finds that mephenesin and acetanilide give false positives with tests of the Udenfriend type, and not with Ehrlich's reagent. But the qualitative test of Hanson and Serin is another matter altogether. It sounds as simple as a Benedict's test for sugar. A blue colour means 5-H.I.A.A. significantly raised: no blue colour means 5-H.I.A.A. within normal limits. With this method, preoperative diagnosis, even in urgent cases of intestinal obstruction due possibly to argentaffinoma, should be perfectly feasible. Difficulties will probably arise in practice, but the method is obviously a very promising one.

Dr. Curzon's own method, which also uses Ehrlich's reagent, breaks new ground with the use of salt solutions for very rapid paper chromatography. It is a remarkably quick method for its class, and has all the advantages of chromatography in the accurate identification of individual compounds; but it can hardly be done, we would imagine, in much under two hours, which makes it considerably slower than Szoerdsma et al.'s method and completely outpaced by Hanson and Serin's.

At the moment, any laboratory undertaking this estimation should be prepared to use any of three methods: (*a*) Hanson and Serin's rapid method for screening (presuming, of course, its value is confirmed); (*b*) one of the extraction methods, to give a quantitative result; and (*c*) one of the chromatographic methods, to make certain that the material extracted in (*b*) is in fact 5-H.I.A.A. It would be unwise to abandon chromatographic methods altogether until we know a great deal more about the mode of excretion of indole derivatives or about possible interfering substances, especially if methods as simple as Curzon's prove adequate.

An incidental point mentioned by Hanson and Serin is the appearance of a red colour in the urine of 3 of their patients. The nature of the pigments concerned has not been established. Presumably some unsuspected reaction of the indole derivatives present is involved, and its elucidation may well uncover facts of interest.

The systemic disturbances associated with argentaffinoma have sometimes been connected with the taking of food [8] and alcohol.[9] In a third paper published this week, Dr. Bleehen records a case of argentaffinoma in which paroxysms of flushing, dyspnœa, and diarrhœa were provoked by fatty food. The attacks regularly followed five to fifteen minutes after a fatty meal. This could not have been a direct action and there must be an intermediate hormonal mechanism—very like the secretin mechanism. What stimulates the tumour cells may stimulate normal argentaffin cells; and Dr. Bleehen's observations may prove of considerable physiological interest.

## NEW MINISTER OF HEALTH

Mr. R. H. Turton has been appointed Minister of Health in succession to Mr. Iain Macleod, who has held office since 1952.

Mr. Turton, who is 52, has sat in the House of Commons since 1929 as Conservative member for Thirsk and Malton. He was educated at Eton and Balliol College, Oxford, and was called to the Bar, Inner Temple, in 1926. At the outbreak of war in 1939 he joined the 4th battalion of Green Howards and he served as D.A.A.G. 50th(N) division and as A.A.G. at general headquarters of the Middle East Forces. He was awarded the Military Cross in 1942.

In 1951 he was appointed parliamentary secretary to the Ministry of National Insurance, and he continued to hold this post when in 1953 the Ministry added pensions to its responsibilities. Just over a year ago Mr. Turton was moved to the Foreign Office as one of the joint under-secretaries of State.

The medical profession will wish Mr. Macleod well in his new office as Minister of Labour. He deliberately made the years which he spent at the Ministry a time of consolidation for the National Health Service. They were also a period of steady if uneventful progress. His successor faces a year to which the imminent report of the Guillebaud Committee is likely to bring incident and, t is to be hoped, opportunities for further advance.

1. Dobyns, B. M. *Endocrinology*, 1953, **52**, 705.
2. Dobyns, B. M., Wilson, L. A. *J. clin. Endocrin.* 1954, **14**, 1393.
3. *Ibid*, 1955, **15**, 1239.
4. See *Lancet*, 1954, ii, 372, 958.
5. *Ibid*, Nov. 12, 1955, p. 1020.
6. Goble, A. J., Hay, D. R., Sandler, M. *Ibid*, p. 1016.
7. Szoerdsma, A., Weissbach, H., Udenfriend, S. *J. Amer. med. Ass.* 1955, **159**, 397.
8. Thorson, A., Biork, G., Björkman, G., Waldenström, J. *Amer. Heart J.* 1954, **47**, 795.
9. Snow, P. J. D., Lennard-Jones, J. E., Curzon, G., Stacey, R. S. *Lancet*, 1955, ii, 1004.

# Special Articles

## CLINICAL PATHOLOGY

### The Challenge of the Future *

E. N. ALLOTT
D.M., F.R.C.P., F.R.I.C.
GROUP PATHOLOGIST, LEWISHAM GROUP LABORATORY, LEWISHAM HOSPITAL, LONDON

ALTHOUGH clinical pathology has been recognised since 1948 as a full specialty in status equal with other specialties, the innumerable discussions about the desirability of a College of Pathology, and of higher qualifications for pathologists, and much of the evidence given before the Hadfield Committee, indicate dissatisfaction and frustration among some pathologists. In my opinion the cause is largely a matter of mental outlook, and the remedy an alteration in outlook among some of the dissatisfied. Such things as higher degrees and diplomas have their convenience in labelling people who have attained a certain degree of proficiency in their specialty, though they should never be used as a criterion for a consultant status; but they will not in any way cure the dissatisfaction referred to, nor raise a person's standing, in the profession, above that established by his own qualities. The standing of an individual can be raised only by himself.

#### Rôle of the Clinical Pathologist

The rôle of the clinical pathologist is twofold.

First he must see that proper investigations are carried out accurately to produce the data required, making full use of the scientific and technical staff of his laboratory. Although he may delegate much of this work to technicians, he must be technically competent to supervise this routine work, and to suspect and rectify errors which may occur.

Secondly he must bring his knowledge of scientific medicine to all types of clinical problem. (By reason of his training and continued scientific outlook, his knowledge of scientific medicine should be greater than that of the average clinician.) He must look at the patient as a whole and endeavour to interpret his findings in the terms of derangement of structure and function. (He must not accept as a fact that the blood-plutonium is raised in the Smith-Jones-Robinson disease, but must continually be asking himself "why?" and trying to find the answer.) He must continually keep in touch with the developments in scientific medicine by wide reading, by attendance at meetings, by visits to other hospitals and laboratories when opportunity offers, and by any other available means.

In my first hospital laboratory appointment in 1928, when the tempo and range of laboratory work were very different from now, the senior surgeon came into the laboratory and asked me about a patient on whom we had done some investigations but whom I had not seen. He expressed surprise, saying "I thought you saw all patients on whom you did tests." Even in those days this was an ideal impossible to realise fully; but the closer we can approach to it, the better will be our work, and the greater its value to our colleagues in other departments.

One of the problems in which the aid of the clinical pathologist is increasingly sought is the control of the electrolyte balance; and here it is particularly necessary to consider the patient as a whole, and not merely the laboratory findings.

For instance, a patient who had had a gastrectomy became ill: she began to froth at the mouth, had generalised twitching, became stuporose, and had an epileptiform fit.

The serum-electrolytes gave the phenomenally abnormal figures of Na 91 m.eq., Cl 60 m.eq., $HCO_3$ 22·3 m.eq., and K 5 m.eq. per litre, with a normal urea level of 27 mg. per 100 ml. (I should say here that these estimates were repeated and found accurate, but they are far the lowest I have ever encountered.) At first sight from these laboratory findings it might appear that there was a gross salt deficiency, and that massive salt therapy was the correct treatment. Further inquiry, however, showed that the patient had been given tap-water per rectum, ad lib, and had absorbed in the previous thirty-six hours the enormous amount of more than 13 pints. It was clear then that the condition was one of water intoxication rather than salt deficiency, and the only therapy used was to cut down the fluid intake. In the course of the next four days the excess fluid was excreted, the patient made a clinical recovery, and the serum-electrolytes returned to normal values of Na 146 m.eq. and Cl 98 m.eq. per litre.

Had hypertonic saline been given in amount sufficient to remedy the apparent deficit—as judged from the blood analyses alone, without consideration of the whole clinical picture—it would probably have perpetuated the œdematous state of the tissues, and prolonged, if not prevented, the ultimate recovery.

From time to time I have been asked whether it would not be possible to construct a nomogram, from which could be read off the proper amount of saline solutions necessary to correct a deficiency. This example shows the futility and danger of such an approach: every case of electrolyte disturbance has to be assessed from the clinical as well as the chemical standpoint, and the appropriate repair fluids have to be calculated individually.

It would be possible to go on indefinitely, citing examples of where a laboratory test by itself could lead to erroneous conclusions, but I will mention only two others:

A patient was admitted with the clinical picture of severe scurvy, and was submitted to an ascorbic-acid saturation test, 700 mg. of ascorbic acid being given every morning and the urine examined four to six hours after the test dose. Even after fourteen days no significant ascorbic-acid excretion had occurred, which suggested that the case was indeed one of severe scurvy, as first thought. But the fact that there had been no significant clinical improvement during this period caused this interpretation to be queried, and further investigation showed that the patient was in fact suffering from chronic nephritis, having a very low clearance not only for ascorbic acid but also for urea. Renal efficiency is, of course, a prerequisite for any type of excretion test.

Another patient, presenting with the typical picture of acute pancreatitis, showed a low value for urinary diastase, and in consequence laparotomy was performed and the clinical diagnosis of pancreatitis confirmed. Further investigation then showed that the patient was in renal failure with a blood-urea of 350 mg. per 100 ml.

Both these cases show how misleading a laboratory test can be if considered by itself; and both mistakes could have been avoided if all relevant findings, including the presence of albuminuria, had been taken more seriously.

#### Discrepancy in Laboratory Findings

Although the fundamental characteristic of the clinical pathologist, by which he is differentiated from the various scientific and technical workers in the hospital laboratory, is his medical training and clinical outlook, these are of no value unless the laboratory work is of the highest practicable standard of accuracy.

It is not always realised how hard it is to maintain a reasonable standard. The laboratory surveys organised by Belk and Sunderman [1] in American laboratories in

* From the presidential address given to the Association of Clinical Pathologists on Sept. 30, 1955, entitled "Clinical Pathology, Past and Present: the Challenge of the Future."

1. Belk, W. P., Sunderman, F. W. *Amer. J. clin. Path.* 1947, **17**, 853.

1947, and by Wootton and King [2] in this country in 1952 and 1954, showed the gross errors made by some laboratories—even in routine estimations such as those of blood-sugar and blood-urea. A recent check in which the same serum was examined by six laboratories (in connection with the preparation of reference standards) showed that there is still no reason for complacency. The six laboratories were all places where a reasonable standard was to be expected: yet there were discrepancies. Thus five out of six found a urea level between 50 and 58 mg. per 100 ml., while the other put it at 64 mg.; five out of six found glucose within range 96–110 mg. per 100 ml., while the other's figure was 79 mg.; and there were ranges of 120–129 m.eq. for sodium in five laboratories with 115 m.eq. in the sixth, and 2·9–3·7 m.eq. for potassium, with one value of 2·4. The four laboratories producing results outside the general range were different for each test.

Variations can, of course, be due to the use of different methods, and a laboratory is usually rather more consistent in its own results than in comparison with other laboratories. (Thus in the 1954 trials organised from Hammersmith [2] the ratio between determinations of the same constituent at different levels showed rather less scatter than the individual determinations.) But, even to maintain internally consistent results, numerous controls and checks of specimens of known content of the constituent being analysed are necessary, and control charts as suggested by Henry and Segalove [3] should be kept. Standards of known content are now available to all laboratories through the work of the joint committee of the Association of Clinical Pathologists and the Association of Clinical Biochemists.

I cannot do better here than quote Bodansky [4]:

"The precision and accuracy of a clinical biochemical determination are also the end-result of a sequence of many steps, beginning often at the patient's vein. Some of these steps are seemingly trivial, but all are important. The supervising biochemist must exercise constant vigilance over each of these steps. He must guard his technicians against the laxness born of the error that the precision of the determination need be merely as good as the biological variability of the components under analysis. The supervising biochemist, whether his primary training is medical or chemical, should be sufficiently acquainted with the clinical material, so that any seeming discrepancy between the laboratory result and that expected from the patient's condition be immediately evaluated in terms of both laboratory procedures and clinical consideration."

Now the gross discrepancies in laboratory findings refer to constituents which are the bread-and-butter of the ordinary laboratory. If there is such a difficulty in controlling everyday tests, how much are the results going to be worth of tests which may be more complicated and less frequent?

### Organisation of Laboratory Work

This leads to thought about the organisation of laboratory services. Before 1948 many of us hoped that laboratory services could be organised on a national or at least a regional basis; but this was not done, and hospital laboratories, for the most part, are directly under hospital management committees. Thirty years ago it was possible for one pathologist to be reasonably expert in all branches of clinical pathology—but the case is very different now: it is possible for an individual to be adequately trained and competent in the day-to-day work of all the four main branches, but it is very difficult to keep in touch with all the detailed advances going on even in one branch. Yet there is neither enough money nor enough skilled staff to enable specialists in all these branches to be appointed to most groups, even if this were desirable.

For certain types of special bacteriological work the central reference laboratories such as Colindale, and for very unusual blood-group problems the Lister Institute, provide a solution; but for many other problems the specialist services should be much more widely dispersed, so that personal contact between the workers concerned is reasonably easy geographically. The most satisfactory way of doing this is to organise pathological services on the basis of a unit larger than the management committee—a unit large enough to provide for specialist staff in the main branches—and if this could be brought about it would be much less extravagant in staff and expensive equipment than the present attempt to make each management-committee service self-contained. At the same time, I would like to express my personal opinion that the administration of the Public Health Laboratory Service and the hospital laboratory service as two parallel organisations is very wasteful of skilled man-power, and, except for special laboratories such as Colindale, and possibly a very few special epidemiological laboratories, economy could be effected by uniting the two types of work as one service.

Failing this suggested reorganisation, the easiest practicable solution is for pathologists in neighbouring hospitals to work as a team. A desire to be self-sufficient sometimes militates against a close integration at the committee level, but there is no reason why the pathologists themselves should not work together, each being responsible for the day-to-day work of his own hospital, as well as developing a specialty for a larger area. This is in fact done in many areas; but there are still places where time is wasted, and standards sacrificed, because a pathologist tries to deal personally with everything sent in, rather than refer any of the work to a neighbouring laboratory.

### Biochemist and Chemical Pathologist

In this context I should like to refer particularly to chemical pathology. The desirability—alike for accuracy of results and for economy of work—of concentrating special investigations applies particularly to some chemical problems. Unless a laboratory performs a given test sufficiently often and regularly to establish its normal range, and put up adequate controls, results are of little value. Moreover, clinical biochemistry is one of the branches of pathology in which progress is going to be made at an increasing speed, and with many increasingly difficult techniques.

If this demand is to be met, the most pressing need is for more pathologists to be appointed whose special interest is chemical, and who have had adequate training in biochemistry. It is unlikely that in any foreseeable future there will be enough of these—nor is there at present enough special work—to justify such an appointment to every group; but they should be sufficiently numerous to be members of most of the teams I have suggested, and this is far from being the case at present.

In many laboratories the non-medical biochemist is already an important member of the team; but, although in pure research the possession or not of a medical qualification is of no importance, in the clinical laboratory service the position is very different, and the chemical pathologist, by virtue of his dual qualification and clinical outlook, is the proper person to collaborate with the clinicians in all types of metabolic disorder.

It must be admitted that the average general pathologist, without special chemical training, cannot compete technically with a trained chemist; but I am convinced that the tendency of some pathologists to shy away from anything chemical and to hand it all over to the biochemist is entirely wrong, and if this tendency extends widely, it may well lead to the complete splitting off of biochemistry from clinical pathology. This would be a major step towards the destruction of clinical

2. Wootton, I. D. P., King, E. J. *Lancet*, 1953, i, 470; Proceedings of 1st European Congress of Clinical Chemistry, Amsterdam.
3. Henry, R. J., Segalove, M. *J. clin. Path.* 1952, **5**, 305.
4. Bodansky, O. *Ann. Rev. Biochem.* 1955, **24**, 628.

pathology as a specialty, and would be to the great disadvantage of clinical medicine.

Compared with the non-medical scientist, the general pathologist has the great advantage of having been trained in physiology, pathology, and the clinical subjects: his wide general medical reading should keep him in the position where he is able to advise his clinical colleagues as to what investigations are likely to be helpful, even if the biochemist is responsible for carrying out the determinations. The general pathologist need not know much about the techniques of estimating 17-ketosteroids or 17-ketogenic steroids, but he should know what they are and what they indicate, and whether their determination in a particular case is likely to be helpful or merely a waste of the laboratory's time.

Other examples which come to mind are such tests as Wassermann reactions and antenatal blood-grouping. For Wassermanns to be reliable, adequate controls—which take up a considerable part of the time of testing—are necessary; and, unless a laboratory has a good many Wassermann tests each week, technicians' time will be saved, and results will be more accurate if one laboratory does the Wassermanns for two or three. The same remarks apply to rhesus grouping: apart from D-screening, and a general test for antibodies which can be done generally, a laboratory doing adequate Rh grouping must have continuously available and accessible a large number of special sera whose individual characteristics are known, and bloods whose constitution in Rh subgroups and other factors is known; and this is impracticable for the limited amount of work going through any individual hospital.

### Training

The training of clinical pathologists is under consideration by our Committee on Academic Affairs, and is in any case far too wide a question for general discussion here. But there are one or two points to which I would like to refer.

I have laid stress on the need for a clinical pathologist to look at his problems from a broad physiological-pathological point of view; but he cannot do this unless he has accurate data from which to reason. Although the experienced pathologist will delegate more and more of the technical work to scientific and technical staff, he cannot do this with safety unless he has personally practised the ordinary techniques of the laboratory sufficiently to become really familiar with them, and their snags and difficulties: if he is to control the work of the technicians properly, he must understand the theoretical basis and the sources of error of the methods used in the laboratory; and this means that a considerable proportion of his early training should be occupied in acquiring technique.

The importance of adequate academic training for all pathologists was emphasised by our association's original committee on training. It was suggested that a period working in a university science department was desirable: if clinical pathology is to hold its place in the forefront of scientific medicine this is essential, not for the technical knowledge gained but as an introduction to scientific method, and scientific mode of thought, which will fertilise all the subsequent career of the trainee. The chemical pathologist, unless he has already taken a science degree, should have at least a year's training in pure biochemistry in order that his work in chemical pathology may be productive, and our Committee on Chemical Pathology has made a strong recommendation to this effect.

For these proposals to be realised, the authorities will have to recognise these periods as *necessary* parts of training, and to make available posts of registrar or senior-registrar status to be held in a science department. This is administratively feasible, because trainees are all appointed at regional level, and the over-all establishment is regulated by the Ministry itself.

### Ancillary or Consultant?

Although clinical pathology has now achieved a position where its practitioners are financially and in every other respect the equal of their colleagues in the clinical branches, it is still sometimes (though not in any official documents) called an "ancillary" subject—a term which (according to the *Oxford English Dictionary*) means subservient or subordinate. For clinical pathology such a description is outmoded; but it could very easily become accurate; for if a pathologist is content to carry out uncritically (even if accurately) numerous tests ordered by a clinician, and leave it at that, he may be a specialist but he is in no way a consultant, and he remains subservient and subordinate. In such a case the years of medical training are wasted and the work could be done equally well by scientific officers and technicians.

If, however, the pathologist takes full hold of the opportunities offered, and, continuing his studies of fundamental physiological and pathological problems, becomes a real medical scientist with a deep and increasing knowledge of disease in the widest sense, applies this knowledge to clinical problems and as far as possible contributes to new knowledge by his own work, his position is totally different: he will be consulted and respected by consultants in other branches, and his status and the future of his subject will be assured. This is a challenge which we all must accept—and on our answer depends the future of our specialty.

---

## "MINIMAL" TUBERCULOUS LESIONS

Sir GEOFFREY MARSHALL presided over the seventh quarterly clinical forum, arranged with the coöperation of Dr. F. B. Kiernander, which was held at the Ciba Foundation, London, on Nov. 28 and was devoted to the Treatment of Minimal Tuberculous Lesions of the Lung.

Prof. J. W. CROFTON emphasised the reduction of the relapse-rate by long-continued chemotherapy. Air Commodore C. A. RUMBALL discussed the reactivation of pulmonary tuberculosis in air-crew by the stretching of lung parenchyma during rapid or explosive decompression or radial acceleration. Between 40% and 50% of nodular lesions resected after chemotherapy, he said, contain viable bacilli, and because of flying stresses such nodules are a greater potential danger to air-crew than to civilians. At present the only acceptable treatment for this type of disease in air-crew is surgical resection.

Mr. J. R. BELCHER said that resection is the only correct operation for these solid lesions: collapse therapy is useless. At the present time he advocates preoperative chemotherapy for six to nine months. His present indications for operation are: (1) breakdown following prolonged chemotherapy; (2) persistently positive sputum; (3) "large" tuberculomas; and (47) where the diagnosis is in doubt. In addition he felt there are still indications for an "insurance operation"—which results in no deformity and can be performed in one stage—for those who are unable to spend a long time in hospital, for those who are apt to forget to take their chemotherapy, and (because of their susceptibility to the disease) for Negroes and recent emigrants from Ireland.

Prof. ROBERT CRUICKSHANK pointed out that all the antituberculous drugs act on the actively multiplying bacilli. Isoniazid is exceptional in that it acts equally well on intracellular organisms. He discussed conflicting views on the effect of chemotherapy on the development of immunity in tuberculosis. In the discussion, Dr. J. L. LIVINGSTONE spoke of the differences in pathology and behaviour of these minimal lesions. Sir GEOFFREY

TODD said that it is now the policy of the Royal Air Force to treat actively all these cases with rest and chemotherapy, with additional resection in selected cases: the optimal period for chemotherapy is still in doubt. The relation of chemotherapy to the development of immunity in experimental tuberculous infection of the cornea in mice was discussed by Prof. J. M. ROBSON. Prof. ROBERT KNOX strongly advocated the administration of rotating pairs of drugs, rather than the continued use of any two of the three principal drugs. Dr. D'ARCY HART referred to the occasional difficulty in deciding whether these lesions are primary or secondary. Mr. VINCE POWELL said that it is often difficult to differentiate between a cavity and an emphysematous cyst occurring beyond fibrosis in cases that have received chemotherapy for a long time.

## A.M.A.'s BOSTON MEETING

THE clinical meeting of the American Medical Association was held in Boston from Nov. 29 to Dec. 2.

In different halls at the same time Dr. PAUL D. WHITE (Boston) outlined the epidemiology of cardiovascular disease, Dr. SHEILA SHERLOCK (London) described the benefits of dietary-protein withdrawal in the treatment of hepatic coma, and Dr. H. M. LEMON (Boston) claimed prolonged remissions of advanced mammary cancer following cortisone therapy. Simultaneous counter-attractions were a sound film by Dr. JOHN C. MATT (Tulsa, Oklahoma) demonstrating the Rizzoli-Stone operation for correction of anovaginal atresia, and a colour-television programme on carcinoma of the stomach by Dr. RICHARD H. SWEET (Boston).

Dr. P. HENNEMAN, from Dr. Fuller Albright's laboratory in Boston, advocated oral sodium phytate in the treatment of hypercalcæmia and hypercalcuria of sarcoidosis, hypervitaminosis D, and idiopathic hypercalcuria. Acting like a resin, it prevents the absorption of calcium by forming insoluble calcium phytate in the gut.

Dr. M. S. SACKS (Baltimore) analysed 42 cases of idiopathic thrombocytopenic purpura; whereas cortisone was of benefit in the acute disease in childhood, it was of little value in the chronic disease in adults.

Dr. F. C. LOWELL (Boston) discussed the significance of smoking as a causal factor in emphysema, and emphasised the smoking habits of his patients by calculating their "cigarette-packet years." His patients with emphysema had a higher incidence of peptic ulcer and bronchial carcinoma than control groups, but the total numbers were too small to indicate anything more specific than a trend.

Dr. G. S. MYERS (Boston) underlined the importance of seeking mitral stenosis in patients with symptoms of chronic pulmonary disease.

Dr. J. L. POOL (New York) demonstrated the difficulties sometimes encountered in differentiating lipoid pneumonia, due to aspiration of paraffin inhalants, from lung cancer.

Dr. BELTON BURROWS (Boston) outlined the response to radio-iodine treatment in a group of 72 patients with hyperthyroidism. Two-thirds responded to a single dose of 10,000 r.e.p.; and, of these, 2 became myxœdematous. In the patients who received multiple doses of radioactive iodine, there was an increased incidence of progressive exophthalmos, and pretibial myxœdema developed in 3.

Dr. SEYMOUR J. GRAY and his co-workers (Boston) discussed the clinical use of urinary uropepsin excretion in gastro-intestinal and endocrine disease. There was a significant difference between the high values in patients with bleeding gastric or duodenal ulcers and the low values in patients with hepatic cirrhosis and bleeding œsophageal varices.

Antibiotics received due attention in a panel on antimicrobial therapy conducted by Dr. CHESTER S. KEEFER, Dr. LOUIS WEINSTEIN, Dr. MAXWELL FINLAND, Dr. CHESTER W. HOWE (Boston), Dr. WILLIAM P. BOGER (West Point, Pa), and Dr. MARK H. LEPPER (Chicago), and also later in a discussion on empyema thoracis by Dr. D. MILLER (Burlington) and Dr. J. P. LYNCH (Boston).

Cortisone was advocated in the treatment of check-rein shoulder, emphysema, and advanced mammary cancer; and there was a panel discussion on cortisone and allied compounds in the treatment of infectious, arthritic, malignant, and degenerative diseases. This was conducted by Dr. R. G. SPRAGUE (Rochester, Minn.), Dr. B. F. MASSELL (Boston), Dr. J. H. BUNION (Bethesda), Dr. O. H. PEARSON (New York), and Dr. W. E. HERRELL (Lexington).

Since Boston is just recovering from a severe epidemic of poliomyelitis, it was appropriate that a session was devoted to discussion of this disease by Dr. CHARLES A. JANEWAY and his colleagues (Boston). On another day Dr. T. H. WELLER (Boston) discussed the enteric viruses.

Dr. EDWARD H. KASS (Boston) revealed that symptomless infections of the urinary tract had been found in about 6% of random samples of outpatients attending the Boston City Hospital on account of other disorders.

## SCOTTISH LAW ON MENTAL PATIENTS

THE Royal Commission set up last year, under the chairmanship of Lord Percy of Newcastle, to inquire into the certification and detention of mental patients in England and Wales [1] has not yet reported. Meanwhile proposals for revision of legislation in Scotland are set out in a white-paper.[2]

The position in Scotland was reviewed in 1946 by the Russell Committee,[3] which laid great weight on voluntary admission. The white-paper now proposes a general simplification of the law; and it suggests a new procedure for the mentally ill patient, dispensing with the need for a judicial order where the patient at present has to be thus dealt with solely because he is not mentally capable of seeking treatment voluntarily. All the proposals are put forward as the basis for discussion, before new legislation is drafted.

### MENTAL ILLNESS

*The Voluntary Patient*

At present the written assent of a commissioner of the General Board of Control must be obtained within three days of a voluntary patient's admission. The white-paper proposes that this procedure should be replaced by a simple notification of admission to the board in the case of patients over 16 years of age; but for those under 16 written assent will still be required. It is proposed to repeal the limitation of the existing provisions which do not authorise the admission or continued detention of a voluntary patient whose mental condition is certifiable.

*The Recommended Patient*

The white-paper proposes that provision be made for a new class of mental patient—the "recommended patient"—who would be admitted to hospital under an intermediate procedure. This new procedure would cover cases where the patient himself is incapable of deciding or is unwilling to enter hospital voluntarily, but the appropriate relative (or in his absence the authorised officer) is willing that admission should be sought in accordance with two medical certificates recommending

1. See *Lancet*, 1954, i, 353.
2. The Law relating to Mental Illness and Mental Deficiency in Scotland: Proposals for Amendment. H.M. Stationery Office. Pp. 14. 9*d*.
3. Report of the Committee on the Scottish Lunacy and Mental Deficiency Laws. H.M. Stationery Office, 1946. See *Lancet*, 1946, ii, 166.

inpatient mental-hospital treatment. The medical superintendent of the mental hospital would have to certify to the General Board of Control within fourteen days of admission that the patient had mental illness and was a proper person to be detained. Thereafter the patient would be protected by safeguards which already apply to certified patients; and, in addition, he would have the right to appeal to the Board of Control at any time within a month of his admission.

*The senile patient.*—Certain aged persons have a type of mental illness that requires mental-hospital treatment. In such a case judicial order can at present be avoided only by voluntary admission. Where the patient objects, or is incapable of assenting, to this course, but the relatives agree that mental-hospital treatment should be sought, the proposed new procedure would enable such treatment to be obtained without judicial process. The proposed new form of certification, says the white-paper, should minimise any risk of senile patients being committed to mental hospitals simply because they need some kind of institutional care. "But the ultimate safeguard must lie in the provision of adequate accommodation for senile patients both in non-mental hospitals and in homes for the infirm."

*The Certified Patient*

It is expected that the great majority of mental-hospital patients will be admitted either as voluntary patients or as recommended patients; but it will be necessary to retain a form of judicial retention. It is proposed that the terms at present in use in the Acts relating to the certification of a person as a lunatic, an insane person, an idiot, or a person of unsound mind should cease to be used. A person could instead be detained in a mental hospital on the order of a sheriff, after certification by two doctors that this is necessary for him to obtain the care and treatment he requires.

MENTAL DEFICIENCY

The certifying doctor, instead of classifying a mentally defective person into one of the present four statutory terms, will be required to state that the patient is mentally defective, and to answer specific questions designed to ascertain what type of provision, training, and accommodation will best suit the patient.

ABSENCE WITHOUT LEAVE

The white-paper proposes that it shall be an offence to assist a certified mentally ill patient to absent himself without leave, knowingly and wilfully to harbour or conceal such a patient, or to assist such a patient to break any condition of temporary leave of absence; or to harbour a certified mentally defective person who is absent without leave from an institution or from guardianship (it is already an offence to assist such a person to absent himself without leave, or to break any condition of his guardianship or release on licence).

# In the Mental Hospital *

## PATIENT AND NURSE

### Effects of Environmental Changes in the Care of Chronic Schizophrenics

J. L. CAMERON M.B. Glasg., D.P.M.†
R. D. LAING M.B. Glasg., D.P.M.
A. McGHIE M.A. Glasg.†

*From the Department of Psychological Medicine, University of Glasgow, and Glasgow Royal Mental Hospital*

FOR a long time many have recognised that the familiar picture of the chronic deteriorated schizophrenic is not a necessary consequence of an inexorable process: even in the most disturbed wards of mental hospitals, occasional spontaneous remissions occur. In the last quarter-century more and more people have come to see that the hospital atmosphere, enforced inactivity, and lack of responsibility can hinder rather than help the patient's progress, and various efforts have been made to modify hospital care accordingly. Believing, with Adams,[1] that the most important therapeutic element in the environment is the people in it, we have attempted an experiment in which a group of patients and nurses were given a chance to develop more or less enduring relationships with one another. This is an account of what happened over a year.

THE BEGINNING

For six weeks one of us spent an hour or two every day in the most refractory female ward of the hospital. This ward houses 65 patients and is staffed by four (sometimes only two) nurses. Some of the patients who were exceptionally noisy and violent, tended to absorb the energies of the nurses. Other patients were habitually passed over, and had very little personal contact with nurses or other patients. They sat round the walls, or lay on the floor, in the same place every day. Occasionally one of them would attack another patient or a nurse, for no known reason, and then revert to her customary inactive state. If approached, several of them were liable to spit obscenities, or to attack one. For this reason they were very seldom approached.

From this group the observer selected 11 patients. The people chosen were at all times confined to the ward, or to a courtyard annexed to the ward, unless visitors came to see them. It was felt that they were all too "disturbed" to attend hospital dances. No occupational therapy was available in the ward. Occasionally someone tried to sew or make a rug, but another patient would interfere and nothing came of it. The only criterion of selection was the patients' social isolation. Their ages ranged from 22 to 63 years, and all had been in the same ward for over four years without even temporary remission. They were all schizophrenics.

During the initial period some changes were made among the patients selected. 2 who were unwilling to go over to the room in which the experiment was to be conducted were replaced by 3 others at the request of a senior doctor. Four months after the scheme had started a patient who had been asking repeatedly to go over was included in place of one who had been uninterested.

The matron delegated two nurses whose sole job was to be with these 11 patients in the room set aside for the experiment. This was large, bright, newly decorated, and comfortably furnished, and it contained magazines and materials for knitting and sewing, making rugs and baskets, drawing, and so forth. The room adjoined a kitchen, a billiards-room used by the staff, and a doctor's bedroom. A door at the head of a stair leading from this block of rooms could be locked or kept open as desired.

We gave the nurses no direct instructions except to ask for daily reports to be written, and sociograms to be completed. We met them once a week to exchange information about the patients.

SETTLING DOWN

The procedure on the first day became the routine which has persisted to the present.

The nurses appeared for duty on the ward at 7.30 A.M. They shared general ward duties until 9 A.M. when they took

* A group of articles chiefly concerned with the value of active occupation and work for mental patients and the means whereby it is best provided.

† Working with a grant from the Scottish Hospitals Endowments Research Trust.

1. Adams, E. C. Cited by Enelow, A. J. *Psychiat. Quart.* suppl. 1, 1954, 26, 44.

their patients over to "the room" where they stayed with them until they took them back to the ward for lunch at noon, leaving them there, while they had their own lunch. At 2 P.M. they collected them again from the ward and took them back to "the room" until 5 P.M. The nurses then returned to "the room" for about half an hour to write up the day's happenings. They did this five days per week and had no other duties. Thus the patients spent six of their thirteen day-hours in the room with their nurses. One or other of the doctors visited the room, at any time, each day, and usually did not stay longer than thirty minutes.

At first "the room" was little more than an extension of the ward. The patients quickly settled into their own jealously guarded places in the room. The nurses put a magazine on a patient's lap, or offered a ball of wool, but the patients remained apparently indifferent and withdrawn. However, several of them began to sew, or read a little. One began to draw. When they returned to the ward they seemed to become entirely absorbed into their customary rôles. From the second morning, however, they were waiting at the ward door to be taken across to the room.

In the first few months, the two nurses devoted themselves to getting the patients to do things or to stop doing things. They used direct exhortations and expressions of approval, or direct prohibitions and expressions of disapproval. They tried to encourage the patients to copy them. They expected their efforts to be assessed by others, and made their own assessment, in terms of whether they got a patient to pick out skeins of wool, or to start a rug, or to read a magazine; or, in terms of whether they were quieter and "better behaved"—e.g., used less obscene language. To a patient sitting with legs up on a chair, they would say, "That's not nice, that's not lady-like." They attempted to instil into them more "correct" table manners: they told them to be "less selfish."

They expressed anxieties that a patient might run away while they were shepherding them from ward to room or back again. They were afraid that in this interval they couldn't "keep a grip on them." They heavily sedated the patients before going over to the room; and they kept the stair door locked. If a patient went outside the room door, they ran after her to bring her back. They wanted to know what to do if a patient started to break up a chair, or to attack another patient.

The nurses felt that the patients were "better" in the room—i.e., quieter, and doing something—but Sister reported that they were "twenty times more uncertain" on return to the ward, attributing this to their resentment at coming back to the ward. It was said that the presence of the doctor, either in the ward or in the room, made them "more uncertain."

### PROGRESS INSIDE THE ROOM

Gradually, however, a change became noticeable in most of the patients, more apparent in the room than in the ward. They paid more attention to their appearance, and some began to sew, draw, or make rugs, with some application. Most of them took over small jobs which they jealously insisted on doing themselves. Thus at tea-time one patient made the tea, another laid out the cups, a third put the sugar on the table, another the milk, yet another spread the tablecloth, and so on.

Some patients began to behave towards one another in differentiated, individuated ways, and there was a certain constancy in these responses.

The nurses were less worried and less on edge. They both felt that the patients were becoming more "sensible." From a survey of what the patients were saying at this period, however, it is clear that the change lay with the nurses, in that they were beginning to understand the patients better. They ceased always to lock the stair door, and to feel it necessary for the patients to be sedated in the mornings. They began to report more phenomenological material. They became more sensitive to the patients' feelings and more aware of their own anxieties.

### VENTURING OUTSIDE

The senior nurse left during the eighth month of the work, and was replaced by another. The day after her departure there was a clear change in the patients. When we came in one of them at once approached us in a smiling and dignified manner. With extreme formality she shook hands and invited us to sit down, at the same time expressing delight at our visit. Most of the patients greeted us in this way. Nearly everyone in the room was knitting or sewing. The patients began to help each other in small ways. Such friendliness became so commonplace that the nurses ceased to make special note of it. But, despite this alteration in social conduct, the patients' speech was still that of severely disturbed people.

The door on the landing was now left permanently open, and the patients began to follow the nurses whenever they left the room on errands. When the nurses started to polish floors the patients began to help them. The nurses' reports at the weekly discussions showed an increasing attempt to understand the patients. The nurses were less concerned with the prohibition of unwanted or antisocial activities by direct action, and more interested in anticipating the unsatisfied needs which they thought produced them.

The patients did more and more of the work in the room, and gradually took over the scullion work in the divisional kitchen. The domestic staff there responded warmly to this unexpected assistance, and regularly we began to find two of the patients there for the greater part of the day. One patient began to scrub the stairs, and another polished the linoleum on all the landings. At first when patients left the room they had wandered erratically through the hospital, but now it was obvious that they were on their way to do something—to collect stores, to clean some part of the hospital, or to go for a walk in the grounds. This movement out of the room was followed by the first requests for weekend passes.

### ADVANCES AND SETBACKS

The next step came when the Matron provided some money to be used by the nurses as they thought fit. Trips into the town for afternoon tea became a regular event, and the patients bought sweets, cosmetics, and materials for home permanent-waves. The nurses reported that the patients no longer merely made small friendly gestures, but helped each other with their hair, with their clothing, or with their self-appointed tasks.

The next change was the introduction of cooking facilities. There was an old gas-oven in the kitchen and the utensils for baking were supplied. All the patients were interested. Some who had not previously joined in any general activity began to help.

About this time the hospital occupational therapists began to attend the weekly discussions. They asked how the nurses managed to get the patients to do so much to assist them. The reply was "We never tell them to do anything. Now, when we are doing something the patients come over to see what it is. Then they start to help, and often take over the entire job themselves. When we have a lot to do we sometimes ask for assistance as one would do among any group of people. It is not a good idea to try to get them to do something just for the sake of doing something."

The general behaviour of the patients continued to improve. There were fewer reports from the ward of the patients attacking others. The nurses from the refractory ward reported that they were receiving more help from the patients, and seemed to feel that they were making good progress.

There was a setback when one of the regular nurses left for four weeks' holiday and a substitute came in

her place. The patients became more easily upset and quarrelsome. Housework and baking stopped. The landing door was usually locked. No-one went out for walks, alone or accompanied. The remaining regular nurse was sharper with the patients and checked them much more, as she had done when she first went to the room. When she too was going on holiday for a fortnight, the newcomer felt unable to carry on, and the room had to be closed for a week. But during this break the patients did not fade into the background of the refractory ward as they had done at the beginning of the scheme. Some of them worked in the ward and others went down to the occupational-therapy department.

On the return of their usual nurse the patients settled down again. During a fortnight when she worked alone in the room further improvements were noted.

The most significant are not however the easiest to describe. For instance, Mrs. Smith said to one of us at tea-time: "Would you care for a cup of tea?" He accepted and she began to pour him a cup. Nurse asked her if the doctor took sugar and milk. "Of course he does. One spoonful of sugar. Don't you remember. He always does." This ordinary conversation, was quite startling both to the nurse and the doctor. Not only was the patient talking sense in sound syntax (this she had done before); but, suddenly she had abandoned the stilted intoning of words which had characterised her speech for years, which is so characteristic to psychotics and so elusive to written description.

### THE ROOM AND THE HOSPITAL

We did not suggest a special name for the scheme, and the nurses named it the "rumpus room." To begin with they had mixed feelings, about it; they regarded it as part of a mysterious and new-fangled series of innovations started by the doctors, but they also took it as a challenge. They felt that they were being given a chance to show what a high standard of nursing in good conditions could do for patients.

The problems which arise when a patient is felt to be "special" caused difficulty. Comments that all the "rumpus room patients" were being specially treated were common among the staff. The group nurses, who did not work on a shift system but were free in the evenings and at the weekends, were considered to have a cushy job. The group nurses reacted in a defensive way to this, adopting a protective attitude when their patients were criticised during staff discussions. Accordingly, reports of the patients' behaviour were often conflicting.

Tensions of this kind are lessening. A change was first noticed when the Matron made available money for trips out. Soon after this it was noticed that the term "rumpus room" fell into disuse.

### DISCUSSION

In the twelve months described many changes occurred in these patients. They were no longer isolates. Their conduct became more social, and they undertook tasks which were of value in their small community. Their appearance and interest in themselves improved as they took a greater interest in those around them. These changes were satisfying to the staff. The patients lost many of the features of chronic psychoses: they were less violent to each other and to the staff, they were less dishevelled, and their language ceased to be obscene. The nurses came to know the patients well, and spoke warmly of them.

We started this work with the idea of giving patients and nurses the opportunity to develop interpersonal relationships of reasonably enduring nature. A physical environment was supplied which was clean and pleasant: and materials for knitting, sewing, and drawing, a gramophone, foodstuffs, and facilities for cooking were made available, and the patients and nurses were left to make what use of them they wished. But our observations on the results seem to us to support the view that what matters most in the patients' environment is the people in it. The nurses found it useless merely to try to get the patients to do something; but, once the patients liked the nurses, attempts to help them became the basis for apparently autonomous activity in which the patients used the material in the environment. Disturbance and rupture of the relation, perhaps because of the absence of a particular nurse, or to some failure in her understanding interrupted this activity.

The material used or the nature of the activity was of secondary importance. Some of the patients improved while they scrubbed floors; others baked, made rugs, or drew pictures. We conclude that the physical material in the environment, while useful, was not the most important factor in producing the change. It was the nurses. And the most important thing about the nurses, and other people in the environment, is how they feel towards their patients. Our experiment has shown, we think, that the barrier between patients and staff is not erected solely by the patients but is a mutual construction. The removal of this barrier is a mutual activity.

We wish to thank Prof. T. F. Rodger and Dr. A. MacNiven for advice, assistance, and support in carrying out this work. We are indebted to the Matron and nurses of Glasgow Royal Mental Hospital for their coöperation.

## Parliament

### Breaches of Privilege?

ON Dec. 19 Lieut.-Colonel MARCUS LIPTON brought to the Speaker's notice two alleged cases of breach of privilege.

The first arose from the publication of a booklet by the British Medical Association, *Homosexuality and Prostitution*, which contained the following paragraph:

> Other ways in which male homosexuals arouse the hostility of the public include their alleged tendency to place their loyalty to one another above their loyalty to the institution or government they serve, and, on the part of homosexuals in positions of authority, to give preferential treatment to homosexuals or to require homosexual subjection as expedient for promotion. The existence of practising homosexuals in the Church, Parliament, Civil Service, Forces, Press, radio, stage and other institutions constitutes a special problem.

In the present state of the law, Colonel Lipton held, any assertion of the existence of practising homosexuals in Parliament must be regarded as serious.

Varying reports of the contents of this publication appeared in the London morning papers on Dec. 16, but the booklet itself was not generally available to the public at bookshops or bookstalls. He had had to obtain a copy from the offices of the British Medical Association, which made it impossible for him to bring up the matter at the opening of parliamentary proceedings that day.

The SPEAKER replied that, in matters of privilege, his duty was confined to seeing whether the conditions were fulfilled which enabled a complaint to get precedence over the orders of the day. One of these conditions was that the complaint must be made at the earliest possible moment. He had ascertained that the report of which Colonel Lipton complained was published on Dec. 14, and extracts from it, including the passage complained of, appeared in the Press on the morning of Dec. 16. Therefore, by the rule, Colonel Lipton ought to have produced it at the beginning of business on Dec. 16 in order to get precedence over the orders of the day. That did not, Mr. Speaker added, prevent Colonel Lipton from putting down a motion for the consideration of the House, which was the final guard of its own privileges.

The second case which Colonel LIPTON raised, dealing with an article on the report in *The People*, was also after consideration disallowed by the Speaker on the ground that only a cutting, and not the whole paper, had been submitted.

## QUESTION TIME

### Supplies of Heroin

Replying to a question asking which London hospitals had, in view of the intended ban, increased their normal stocks of heroin, and whether he had approved the additional expenditure thereby incurred, Mr. IAIN MACLEOD, the Minister of Health, said that he regretted that the information was not available. There would, of course, be no question of approval for additional expenditure for such a purpose but authority was not required for the purchase of drugs within the total of the approved budget.

Lieut.-Colonel MARCUS LIPTON: Is it not quite deplorable that a small group of doctors should have made up their mind to sabotage the ban the Government were intending to impose? Is the Minister not going to make clear that further attempts to evade the ban, which the Government are standing by at the moment, will be viewed with disfavour by him?—Mr. MACLEOD: This is a difficult question. We do not control the stocks of drugs which a hospital chooses to purchase, and even after reflection I do not want to issue any form of instruction on this matter: I think that would be going too far. On the other hand, it is right to say that this is an expenditure of public money, and that therefore those who spend it should take into account the views of the Government.

Replying to a further question Mr. Macleod said that heroin addicts were not registered or licensed to receive heroin, and a patient received heroin under the National Health Service only if his doctor prescribed it as being necessary for his treatment. If heroin were not available it would be for the doctor to decide which, if any, of the various alternative drugs should be prescribed.

Dr. DONALD JOHNSON: Will the Minister be mindful of the danger that these people, many of whom are chronic addicts, will form a hard core for the illicit traffic in drugs in the event of heroin being stopped? In particular did the Minister see in *The Lancet* the letter by a medical man in which he mentioned that two of the addicts he was treating had been approached by pedlars in drugs?—Mr. MACLEOD: I saw that letter, which I thought was a very strange one for a doctor to write. I would say that the number of addicts in this country is known to be so small that I do not think they would provide any appreciable traffic in an illicit trade.

Replying to further questions Mr. MACLEOD said that he saw no reason for setting up, under the National Health Service, laboratories for he manufacture of dangerous drugs for distribution to medical practitioners.

### Health Centres

Mr. SOMERVILLE HASTINGS asked the Minister of Health to what extent local health authorities had provided accommodation for general practitioners in premises in which their clinics were held, so that the advantages of close association between services for prevention and cure might be obtained without the cost of new building—Miss PATRICIA HORNSBY-SMITH, parliamentary secretary to the Ministry, replied: The Ministry is not aware of any such cases unless the hon. Member has in mind health centres.

Mr. HASTINGS: Would not the hon. Lady agree with Lord Dawson of Penn that one cannot separate prevention and cure, and is it not desirable, wherever possible—as I believe is being done to some extent in Birmingham—to associate practitioners with preventive services?—Miss HORNSBY-SMITH: The Minister would encourage any experimental scheme for associating general practitioners with the local health services, especially in coördinating antenatal work, provided that it is both legally and financially justifiable. A considerable number of experiments, which vary in their application, are being carried out on the health centre basis.

Replying to a further question Miss Hornsby-Smith said that 6 new health centres had been provided under the National Health Service Act, 1946, in addition to 24 premises taken over as centres by local health authorities in 1948. A 7th new centre was opened recently and a small number of schemes were at various stages of planning and construction. The Minister would continue to support, so far as he could, further experimentation where new facilities for local health authorities and general practice were needed and coöperation between these branches of the service could be achieved.

Mr. ARTHUR BLENKINSOP: Would the Minister be prepared to consider whether any detailed amendment of the Health Service Act might be necessary to encourage coöperation between the preventive and the aftercare services?—Miss HORNSBY-SMITH: The experience of how these new centres work in a year or so after their inception will be of great benefit in judging their future use, but it would be idle to ignore the fact that needs vary from area to area. While these centres might serve a vital need in a new community, they are not always as applicable in old-established residential areas.

### Chronic Bronchitis

Replying to a question Mr. MACLEOD said that he was aware that the death-rate from chronic bronchitis in adult males varied greatly in different localities, and in the same locality in those engaged in different industries. Some aspects of the problem were already being considered by his Standing Medical Advisory Committee and, he was informed, by a working party of the Medical Research Council.

Mr. HASTINGS: Does the Minister realise that the death-rate from bronchitis in this country is higher than in most countries, if not, indeed, in any other country? Does he also realise the number of days' work lost every year through this affection, and is it not time that a serious attempt was made to discover how it can be prevented?—Mr. MACLEOD: Yes, indeed, I feel it is time that we did that, and it is exactly for that reason that the two inquiries I have mentioned have been put in hand. In addition, I am informed that in 1956 the Industrial Health Advisory Committee of the Ministry of Labour is also to take up this problem.

Dr. EDITH SUMMERSKILL: As the mortality-rate from chronic bronchitis is higher in Warrington than in any other constituency in the country, can the Minister say whether the mortality-rate varies in direct ratio to the degree of air pollution?—Mr. MACLEOD: I should not have thought that it was in direct ratio, but there is beyond doubt a connection between the two.

Replying to Dr. BARNETT STROSS, Mr. MACLEOD said that he had noted the encouraging fall in the death-rate from tuberculosis in recent years, but the numbers of new cases notified had not been falling so quickly and still made heavy demands on the chest clinics. He could not accept the suggestion that the death-rate from chronic bronchitis was rising.

Dr. STROSS: If we are successful in further combating tuberculosis, could not the staffs of the chest clinics be used for dealing with chronic bronchitis and allied disorders?—Mr. MACLEOD: The bronchitis figures must be studied with great care, because they are not always comparable owing to the changes in the international classification. It is true that we can look forward to having a considerable increase in resources as the beds for tuberculosis are not so much used, but I do not think that that time has yet come.

### Tuberculosis in Common Lodging-houses

Replying to a question Mr. MACLEOD said that he was aware of the recent evidence indicating that a not inconsiderable proportion of those living in common lodging-houses and reception centres were suffering from pulmonary tuberculosis and liable to infect others. He was considering how best to deal with the matter. He was having a meeting very soon with the Ministry of Housing and Local Government and the National Assistance Board to formulate a joint plan of action.

### Hospital Building

Replying to a question Mr. MACLEOD said that the total estimated value of hospital capital building projects now in progress, or to be started in the current financial year, including projects financed from non-Exchequer funds so far as information about these was available, was about £31½ million.

### Radiation Hazards

Replying to a question asking what action was being taken to ensure the protection of hospital staffs against radiation hazards, Mr. MACLEOD said that the Radioactive Substances Advisory Committee had submitted to him a code of practice for the protection of persons working with ionising radiations in hospitals. This would form the basis of advice which he hoped to send to all hospitals shortly.

Mr. BLENKINSOP: Is the Minister aware that the existing practice varies greatly between one hospital and another in this respect? Would he consult the Minister of Labour about the responsibility for issuing the necessary orders under the Radioactive Substances Act? If it turns out to be his responsibility will he consult himself?

### Albomycin

Replying to a question Mr. MACLEOD said that members of the staff of the Medical Research Council discussed the properties of albomycin with the doctors who recently visited this country from the Soviet Union. The Council were endeavouring to obtain a supply of this antibiotic from the Soviet Union so that its properties could be investigated.

### Old People's Homes

Mr. C. I. ORR-EWING asked the Minister of Health whether he would appoint a committee to inquire into the well-being of old people in homes administered by the local and county authorities.—Miss HORNSBY-SMITH: No, Sir. Homes provided by local authorities under part III of the National Assistance Act are inspected by the Minister's officers from time to time, and he is satisfied that the local authorities are alive to their responsibilities and that the residents in these homes receive a very high standard of care.

Mr. ORR-EWING: Does my hon. Friend not agree that the Curtis Committee does most valuable work for children in public care, and would she consult the Minister to see if a similar committee might be set up to look after the well-being of old people, because there are numbers who suffer from not very good feeding, and numbers of other elderly people who are subject to unnecessarily strict discipline in these homes?—Miss HORNSBY-SMITH: It is only fair to local authorities to say that during the past years they have increased considerably indeed not only the number of beds but also the standard of part III accommodation for old people. Recognising the difficulty that there is a large demand, which they are not always able to meet, they have also done an enormous amount of work in improving the old P.A.I.S. being used for this purpose. It is not possible to give them up because of the demand by the large number of patients. It would be a great reflection on the fine work the local authorities have done in difficult circumstances if any suggestion went out from this House that they are not doing their job fairly.

## Public Health

### New Regulations on Food Hygiene

IN his recent report for 1954,[1] Sir John Charles, chief medical officer of the Ministry of Health, said that the preventive measures which had been taken against food-poisoning had been ineffective. Action to improve the situation has quickly followed. In conjunction with the Minister of Agriculture, Fisheries, and Food, the Minister of Health has made new regulations,[2] which were laid before Parliament on Dec. 21, and most of them will come into operation on Jan. 1. They add a number of new provisions in respect of the hygienic handling of food and the construction and maintenance of premises, stalls, vehicles, &c., where food is handled. Among points referring to food-handlers, any open cut or abrasion must be kept covered with a suitable waterproof dressing, and smoking is barred while handling "any open food" or working in "any food room where there is open food." The regulations prohibit the use of newspaper for wrapping food other than uncooked vegetables. Some foods prepared in catering establishments must be kept at a temperature of not less than 145°F until they are served for immediate consumption. This will be a difficult regulation to enforce, but it should impress on caterers who care little for bacteriology the importance of handling made-up dishes and precooked foods with particular care.

Local authorities can grant certificates of exemption in cases where the regulations cannot reasonably be enforced—for example, where accommodation is restricted. If a certificate is refused or withdrawn, an appeal may be made to magistrates. The new regulations can come into force without affirmation by Parliament.

A statement by the Caterers' Association of Great Britain said [3] that the stricter regulations would cost the hotel catering industry many thousands of pounds. While the association believed that the dangers of food-poisoning in commercial catering establishments had been greatly exaggerated, it was fully alive to the need for the highest standards of hygiene and it will therefore play its part by helping its members to understand and thus comply with the regulations.

1. See *Lancet*, Dec. 17, 1955, p. 1289.
2. The Food Hygiene Regulations, 1955. S.I. 1955, no. 1906. H.M. Stationery Office. 6*d*.
3. *Times*, Dec. 22, 1955.

## In England Now

*A Running Commentary by Peripatetic Correspondents*

How does one address a colleague? The older men, particularly if they are old Furrovians or were up at 'varsity in Edwardian days, are of course mostly committed to surnames, but in recent years there has been, among the younger generation, a vogue for christian names. The radio and television have encouraged this trend, for the announcer's business is to create for both the novice on the air and the listener an atmosphere of informality and friendliness. In hospitals christian names tend to be used if one is fortunate enough to have a lady doctor on the establishment. "What did you think of the case, Dr. (or Mrs. or Miss) Winterbotham" sounds cold and staid: and even had you been of her sex and on the same staircase at St. Borage's you would not want to call her plain Winterbotham. The gentle sex merits a less formal form of address; indeed, the ladies themselves often suggest it. ("In future, call me Penelope," they say.) Then again, christian names are used if Americans are about, or when colleagues have returned to these shores with a fondness for the American way of life. ("Say, meet Al;—gee Al—I'm so sorry, I forget your name although you did tell me once.") Naturally christian names must be reserved for such places as the laboratory, lunch table, or hospital lift and not for the bedside.

For those who wish to adopt the informal mode of address with colleagues of like age there are well-known techniques in common use. A smooth transition from surname to christian name may be effected by letter, at first subtly and by stages in the signature, and then more openly in the form of address, perhaps with an apology—"My dear Ambrose (I am sure you will wish it thus)." Another way is to initiate the change over the telephone when grins, frowns, and blushes are invisible. Or, most gracefully of all, you may effect the change in the man's presence through the mediary of his wife: "I can't recall, does Percy take cream in his coffee?" Thereafter you can call him Percy with impunity.

It is of course easy for a senior to call a junior by christian name and some, even those who qualified pre-1914, now regularly do so maintaining that it encourages better work. It is not so easy, however, when a junior consultant wishes to be on friendlier terms with a chief but ten years his senior. It is generally accepted that the senior man must make the first move, though I know of several successful instances where the junior has seized a convenient moment—at the residents' Christmas party, for instance—and boldly broken the ice with one blow ("Why, Alfred old boy, I've never seen you look better"). The sooner the change is made the better, because as they grow older the age-gap narrows: thus when one of them is 80 the other will be 70, and they will then both be too embarrassed to put the matter right. Incidentally it will act like a tonic if you address an octogenarian, or even a septuagenarian, by his christian name: at this age the dears begin to feel out of the swim, and with so many of their friends of necessity departed they are more lonely than one thinks. They delight at being encouraged into the society of younger men.

Paradoxically enough the difficulty about informality in address is increased when the senior man is knighted and the christian name with the prefix "Sir" now becomes the correct mode of formal address. Dare one drop the "Sir," thinks the junior. This happened to me when my old chief Lethal Chambers, the anæsthetist, was knighted. I thought that "Chambers" would be a good halfway between "Sir Lethal" and "Lethal," but decided eventually to go all out for "Lethal." I am so glad I did because now that he is a peer I feel so much more at home when he has me to tea in the library of the House of Lords.

* * *

As I crawled through the African jungle in my mosquito-boots and topee with trailing chains (a useful prophylactic against sickness), I reflected on the words of my colleagues and friends before I left England: "How lucky you are to be able to get away to a quiet

spot where you can live and work far from the bustle." What nonsense! Life in the tropics goes on at a far faster pace than at home. Everyone seems to delight in violent outdoor exercise in temperatures which were meant for sleep only. There is a constant stream of visitors to be entertained, and dinner parties are almost a nightly event. You have to be a member of two or three clubs and appear there fairly frequently; and I spend a lot of my spare time writing letters home. No, give me the peace and quiet of a London suburb where I am on smiling terms with my neighbours but would never think of visiting them, or they me; where I don't need to entertain my relatives and friends from one Christmas to the next; where my main exercise is turning the knobs of the television set; where the greatest intrusion on my privacy is a telephone call from a friend once or twice a week; and where the only letters I write are replies (after a decent interval) to the anxious ones I receive from my lonely friends in the tropics.

* * *

*The Christmas spirit among hospital administrators?*

Dear Dr. X,

I am writing to you to express the hope that except in case of absolute necessity there will be no further discharges from the wards between now and Christmas Day. I am raising this matter with you because of . . . the undesirability of emptying beds which cannot be filled, thus creating a very bad occupation figure to return in the official statistics which have to be submitted to the Ministry of Health.

Yours sincerely,
Y. Z.,
Hospital Secretary.

* * *

The red stag which visited us before Christmas seems to have come to stay. It is an extraordinary beast. Last week he spent the whole day grazing with the cattle in the meadow behind the farm, and when the old sheep-dog went coursing out to bring the milk cows in at dusk the stag followed them into the shippon. Antlers get a bit in the way with milking-machines, and the visitor was obviously not built for such feminine functions, so George had to push him out and shut the door. Just why a wild red stag should take it upon himself to come down from the hills and masquerade as a shorthorn heifer is wrapped in mystery. Perhaps it is something to do with the gentlemen who dress themselves in skirts and bras and get read about on Sundays. But whatever his clothing, any sort of wolf in his nature would make a most interesting cross. Germany may boast of breeding back to the aurochs, but we look more like achieving the cow that jumped over the moon.

Perhaps he is the odd man out in the musical chairs of last November. I have often met stags in the rutting season and they are unpredictable. I remember one Saturday afternoon at 2000 feet, coming round a summit cairn to find a huge red stag standing on the blind side. It was touch and go who jumped first. Luckily he did, and backwards at that. He bounded down the crags with a much smarter turn of speed than I could have done if it had been the other way round. Maybe our local Rudolph is finding solace in the companionship of some female company that vaguely resemble the unattainable. Maybe he is astigmatic. Who knows? He has thrown to the winds his native caution, almost begging to be shifted off to Richmond Park for photographs and sandwiches. The trouble is that if he hangs around here much longer he risks getting into a sandwich himself. Some people are not averse to dirty work on a dark night, and venison is an acquired taste.

* * *

Father Christmas (to nine-year-old girl after depositing presents on the end of her bed): "Now do you believe in Father Christmas?"

Little girl (fluently): "Yes, Doctor!"

* * *

MINISTERIAL CHANGES

Another Act begins. Ring up the Curtain!
Who's our new Hero now? The name is Turton.
But, doubtless lest the Play might still fall flat,
They've fixed it that our Heroine's still Pat!

# Letters to the Editor

## DOMICILIARY CONSULTATION IN PSYCHIATRIC PRACTICE

SIR,—Dr. Denis Leigh writes (Dec. 17): "It is my experience that a family doctor is well advised to steer clear of psychotherapy, other than simple, supportive measures." This statement in its unqualified form seems to me misleading. It is true only for certain general practitioners who were trained in a certain way and who are working with certain psychiatrists.

Experience in the general-practitioner seminars of the Tavistock Clinic has shown that "simple supportive measures," and especially wholesale "reassurance" and "advice," are hardly more than well-meant shots in the dark which as often as not fall very wide of their targets. I wish to add that ours are not the only experiences of this kind; from all parts of the world research-workers in psychotherapy report similar observations.

It has been stated time and again that at least a third of the general practitioner's work consists in dealing with "neurotic" disorders. To advocate a hit-or-miss therapy for this vast number of troubled patients is unjustifiable.

Admittedly the present training of students does not properly equip them for the task. This, however, can and must be remedied. Psychotherapy must become as integral a part of medical training as bacteriology or pharmacology are already. That this has not yet happened is mainly due to the unduly conservative attitude of the teaching hospitals.

The Tavistock Clinic scheme for general practitioners has shown that in psychotherapy—as in all other branches of medicine—correct therapy can be based only on proper understanding of the patient's problems. With some honest effort the skill needed for understanding the patient's psychological problems can be learnt, to the great benefit both of the patient and of his doctor; for if the problem is understood the development of the frustrating and irritating atmosphere that so often obtains between the neurotic patient and his doctor can be prevented.

A proper follow-up of our cases proved that this better understanding enables the general practitioner to achieve therapeutic results that would be a source of pride to any psychiatrist. I wish to emphasise that the doctors taking part in our seminars become, not amateur psychiatrists, but better general practitioners.

A pre-condition of this development is a change of heart both in the psychiatrist and in the general practitioner. The general practitioner has to give up his safe *status pupillaris*—his being the little man who looks up with ambivalent respect to the great consultant—and the consultant has to divest himself of his aura of omniscient mentor. After that they may settle down to study together an, as yet, hardly explored field—psychotherapy in general practice.

The Tavistock Clinic,
London, W.1. MICHAEL BALINT.

SIR,—Dr. Denis Leigh's efforts to improve the psychiatric service are commendable, but certain of his views are highly regrettable and misleading.

I entirely disagree with his statement that "general practice is not the milieu in which to practise psychotherapy," and I can only conclude that his experience must have been very unfortunate to have led him to believe that "a family doctor is well advised to steer clear of psychotherapy."

I am a family doctor, and it has been my experience that psychotherapy is the most useful form of treatment available in general practice; by its use I have been able to help far more patients than I could ever have done with placebo or symptom-stopping medication.

DIAGNOSES IN 68 CASES REFERRED FOR PSYCHIATRIC OPINION, 1951–53

| Diagnosis | Male | Female | Total |
|---|---|---|---|
| Asthma | 2 | 2 | 4 |
| Anxiety state | 3 | 4 | 7 |
| Anxiety-hysteria | 1 | 3 | 4 |
| *Children:* | | | |
| Behaviour difficulty | 1 | .. | 1 |
| Enuresis | .. | 1 | 1 |
| Truanting | .. | 1 | 1 |
| Depressive state | 4 (1) | 12 (3) | 16 (4) |
| Dyspareunia | .. | 2 | 2 |
| Dementia, arteriosclerotic | 1 | 1 | 2 |
| Hysteria | 1 (1) | 10 (1) | 11 (2) |
| ,, ? terminate pregnancy | .. | 3 | 3 |
| Impotence | 2 | .. | 2 |
| Mania, acute | 1 (1) | .. | 1 (1) |
| Mental deficiency | .. | 1 | 1 |
| Obsessional state | 4 (1) | .. | 4 (1) |
| Psychopathy | 2 | .. | 2 |
| Schizophrenia | 3 | 2 | 5 |
| Ulcerative colitis | .. | 1 | 1 |
| Total | 25 (4) | 43 (4) | 68 (8) |

Figures in parentheses indicate numbers of patients admitted to hospital.

Of course, a proper understanding of the factors underlying psychiatric disturbances is necessary, in the same way that a knowledge of pathology is essential in dealing with physical disease. Just as we talk of "major" and "minor" surgery, so we may talk of "major" and "minor" psychiatry; and I believe that the general practitioner should be able to deal with minor psychiatric problems by means of minor psychotherapeutic measures —and, equally important, he should also have the time. Levine[1] describes twenty-five techniques of psychotherapy which may be used by the general practitioner.

Dr. Leigh's proposal that the family doctor should not undertake this type of treatment suggests that he is not fully aware of the extent of the need for it, and it also implies a very poor opinion of the family doctor's capabilities that I cannot accept. It is the psychiatrist's duty to ensure that doctors-in-training are properly fitted for the work they will find awaiting them.

Dr. Leigh writes: "The general practitioner himself deals with most of his psychiatric patients." This is as it should be—in fact, as it must be when one realises the numbers of patients involved.

In my own practice, in a survey I carried out in 1951[2] I found that 11% of my patients had psychiatric disturbances and a further 31% psychosomatic illnesses, making a total of 42% with illness due to stress.

In the three years 1951–53 I referred 68 National Health Service patients for consultant psychiatric opinion; the final diagnoses are shown in the accompanying table. 26 of these patients were seen on domiciliary consultation, and 8 of them were admitted to mental hospital. I would add that I was present during the psychiatric interview in every case (nor would I have it otherwise), and in no way did this interfere with the patient-psychiatrist relationship as Dr. Leigh seems to expect. My view is that if the family doctor's relationship with the patient is good, then the full history will be ready for the psychiatrist, who can use the time in the diagnostic interview to explore the patient's personality structure and the possible underlying psychodynamics, and to assess the need for treatment and the type of treatment required.

During this same time I saw just over 300 patients with minor psychiatric disorders which I treated without referral for psychiatric opinion, and a much larger number of patients with psychosomatic disorders. All of these required psychotherapy—some of them forming the basis for an investigation into the management of the climacteric.[3] The results of this alone show the value of psychotherapy in general practice.

Although my average list during the three years 1951–53 was only 1350 I still found it difficult to give sufficient time for psychotherapy; so it is hardly surprising that a practitioner with a list of up to 4000 will have time only to treat symptoms, and will not be able to deal with underlying emotional difficulties. This does not mean that this method is unsuitable for general practice—it means that if the general practitioner is to practise with a fully orientated psychiatric approach he cannot have a large list of patients.

Finally, Dr. Leigh correctly criticises the training of the medical student in psychiatry, and he asks: "Can the established practitioner be given further teaching?" I am surprised that he does not go on to answer this question by referring to the paper by Dr. Michael Balint,[4] who has described the method used at the Tavistock Clinic. I am only one of many who have found, and still finds, the weekly seminar a great help, and I can wholeheartedly recommend this course to any doctor who aims to *help* his patients in the fullest sense of the word. Further, I would recommend that psychiatrists throughout the country consider the possibility of arranging this type of seminar for groups of family doctors who are interested in this approach. Perhaps here, more than anywhere, is the opportunity for the general practitioner to practise true preventive medicine.

London, N.W.3. PHILIP HOPKINS.

1. Levine, M. Psychotherapy in Medical Practice. New York, 1947.
2. Hopkins, P. *In* Modern Trends in Psychosomatic Medicine. Edited by Desmond O'Neill. London, 1955; chapter 1.
3. Hopkins, P. *Trans. Hunter. Soc.* 1955, **13**, 89.
4. Balint, M. *Brit. med. J.* 1954, **i**, 115.

## HEALTH CENTRE OR GROUP PRACTICE?

SIR,—The virtues of group practice are not in dispute. Indeed, the Harlow experiment has the merit that it combines the virtues of group practice with those of a health centre. In so far as Dr. Munro and his colleagues (*Lancet*, Dec. 17) in Edinburgh are preaching in favour of group practice, they are preaching to the converted.

Their general argument—that good group-practice accommodation can be provided at two-thirds what it has cost at Harlow—is not unreasonable, though it may prove misleading. Their capital costs were 13*s*. 3*d*. per patient at risk as against £1 per patient at risk at Harlow. To achieve this saving, they reduce consulting-room size, omit alternate examination-rooms and sluice- and specimen-rooms, and get rid of pram shelters. This would certainly not give a 33% saving in a new building. I suspect that the discrepancy between the Edinburgh and the Harlow figures lies mainly in the fact that at Edinburgh it was apparently possible to adapt two buildings without having to build everything specially for the purpose.

Any group practice which is fortunate enough to be able to adapt rather than build afresh may manage to get good accommodation at 13*s*. 3*d*. per patient at risk. Such adaptable premises can usually be found in industrial areas. But at Harlow, and on most new estates, there are no existing buildings to be had; for a completely new group-practice building, it would be unwise to allow less than 17*s*. to £1 per patient at risk.

Had Dr. Munro and his colleagues visited Harlow, most of their criticisms would have been answered.

(1) The Harlow health centres are experimental. So three different consulting-room sizes have been tried. At one health centre the consulting-rooms are 10 ft. by 10 ft.; experience has shown that this is just a little too small. The extra foot or two each way is worth the extra cost.

Experience has also shown the value of one examination-room per consulting-room. Indeed, in our next health centre we hope to have one-and-a-half examination-rooms per consulting-room. Half an examination-room, as Munro et al. advocate, is better than none; but when work is heavy, delays must be inevitab[illegible]

(2) Again, a sluice- and specimen-room is provided in only one of the health centres. So far, our experience suggests that its cost is justified.

(3) The cost of a simple pram shelter is small—about one-tenth of that of an oil-fired central-heating system. It might be classed as a luxury if no local-authority clinics were held in the same building. But Harlow is a "pram-town," and it is usual to see twenty or more prams parked outside a health centre. In these circumstances, to provide a new clinic building without a pram shelter would be unthinkable.

(4) The idea of using the G.P.'s consulting-room for local-authority clinic purposes has its attractions. But there are disadvantages; for example, a G.P. may want to see long cases in the afternoons when the clinics are in action. Moreover, there must be rooms for the midwives' clinics, for the health visitors' weighing and educational sessions, and space for antenatal exercises. Some doubling-up is possible, but there are limits.

(5) Coöperation with the local-authority services is certainly possible without physical juxtaposition. But the advantages of having clinics, health-visitors, district nurses, and the dentists under the same roof have to be experienced to be realised. The estimates of Munro et al. on space required for records and on secretaries and receptionists needed are confirmed at Harlow. But they would scarcely need to pay the salaries of two full-time nurses if the district nurses held daily clinics in their premises.

The points raised by Dr. Munro and his colleagues have been answered in detail to avoid misunderstandings. Adequate new group-practice accommodation can be got a little cheaper than at Harlow, but only by making real sacrifices in efficiency. I am sure Dr. Munro's cost figures are "realistic"; I must ask him to accept that the Harlow figures are no less realistic. As health centres go, the Harlow buildings are among the cheapest ever constructed. It would be a bad day for general practice if the authorities in their future buildings set out to cut on our modest Harlow costs.

This is not to belittle the fine achievement of Dr. Munro and his colleagues. If all doctors in industrial areas and new housing estates would follow their example, the most pressing problem of general practice would have been solved.

Harlow. STEPHEN TAYLOR.

## NON-ANTIGENICITY OF CHONDROITIN SULPHATE

SIR,—Dr. Boake and Dr. Muir (Dec. 10) refer to work by us.[1] We should like to call attention to some facts which have recently come to light in the course of our work, which may account for some of the discrepancies between the two sets of results.

Since our original report we have several times obtained (in rabbits) precipitating sera for cartilage extracts, using streptococcal vaccines coated with human-cartilage extracts prepared by the method of Einbinder and Schubert.[2] We have also noted, however, that antisera to human blood-group A substance (obtained by the same immunising method) give positive complement-fixation tests with some samples of cartilage extract.

Conversely, positive complement-fixation tests have been obtained with antisera to certain human-cartilage extracts and purified human blood-group A substance. Cruickshank,[3] using a precipitin test, has also found cross-reactions between rabbit antisera to human-cartilage extract and human blood-group substances.

From these observations it may be inferred that extracts of cartilage prepared by the method of Einbinder and Schubert sometimes contain traces of blood-group substances, and that it is antibodies to these, and not to the chondroitin sulphate itself, that are obtained.

Another factor which may influence the antibody response of rabbits is the presence of an A-like substance in the tissues of some rabbits. We have described the effect of this factor on the antibody to human blood-group A substance in a paper at present in course of publication.[4]

Canadian Red Cross Memorial Hospital, Taplow, Maidenhead, Berks. L. E. GLYNN
E. J. HOLBOROW.

## FILM ON BLOOD-TRANSFUSION

SIR,—In comment on your review (Dec. 17, p. 1303) of the new film on blood-transfusion, on which I acted as technical adviser, I must point out that the "needle-piercing" set was used in the demonstration deliberately, after consultation with the Ministry of Health, on the grounds that the principle has not been abandoned, and that after suitable clinical trials a similar type of set will (contrary to your belief) be reintroduced by the National Blood Transfusion Service. Furthermore, this film is intended for wide distribution outside this country, where this type of set is almost invariably used.

North London Blood Transfusion Centre, Deansbrook Road, Edgware, Middlesex. J. D. JAMES
Director.

## PROTOPHRENIA

SIR,—Dr. Bourne (Dec. 3) has performed a valuable service in reviving the interesting question whether in some severely afflicted mental defectives the arrested mental development is due to severe and prolonged psychological trauma in early childhood. Apart from the problem of diagnosis, the really important issue is whether, or how far, "protophrenia," as described by Dr. Bourne, is reversible. In his account of some of the older children in his group "some become docile imbeciles, and others burnt out and dilapidated ones; yet others do not change." Dr. Creak (Dec. 17) has pointed out that many such child psychotics, as she terms them, even with intensive psychotherapy do not return fully to normal and some have to be regarded as permanently "atypical."

It is by no means rare in hospital practice to find persons of medium-grade feeblemindedness (e.g., I.Q. 60) who as children were classified as imbeciles and whose behaviour seemed to be consistent with this and, indeed, with that of members of Dr. Bourne's residual group. Yet, in the course of time, changes sometimes occur. For example, a few days ago a 20-year-old girl here was re-tested with the Wechsler scale; four years ago her I.Q. was 37 (i.e., very near the mean of Dr. Bourne's residual group), but it has now increased to 54, with a corresponding improvement in social competence. In the light of experience at this bospital there now seems in her case to be every prospect of some further mental growth. Indeed, our general finding has been that those with the worst social histories tend to have the best prognoses, not only in terms of I.Q. increment [5] but also in their eventual social adjustment.[6]

As yet very little is known about the dynamics and limits of this improvement; but experience suggests that, in the absence of intensive psychotherapy, changes of this nature tend to be delayed until adolescence or even later. These may perhaps occur as a result of only very gradual recovery from psychological injury, because, as Hebb,[7] Eickhoff,[8] and others have indicated, early learning experiences form the basis for subsequent learning. Thus the "protophrenic" may lack the basis for the next step in mental development, with the result that later learning may at the worst not occur, or at the best be delayed and proceed over a long period of time. Eventual improvement in such patients may arise partly as a result of removal from disastrous circumstances and partly as an effect of exposure to new environmental

1. Glynn, L. E., Holborow, E. J. *Lancet*, 1952, ii, 449.
2. Einbinder, J., Schubert, M. *J. biol. Chem.* 1950, **185**, 725.
3. Cruickshank, B. Personal communication.
4. Glynn, L. E., Holborow, E. J., Johnson, G. D. *J. Immunol.* (in the press).
5. Clarke, A. D. B., Clarke, A. M. *Lancet*, 1953, ii, 877.
6. MacMahon, J. F. *Brit. med. J.* 1952, ii, 254.
7. Hebb, D. O. The Organisation of Behaviour. New York, 1949.
8. Eickhoff, L. F. W. *J. ment. Sci.* 1955, **101**, 399.

conditions for varying periods of time, which may include education or training. We do not know, however, what proportion of such children are even capable of subsequent improvement, and thus it is to be hoped that the Fountain Hospital will report from time to time the progress or otherwise of Dr. Bourne's residual group.

The Manor Hospital, Epsom, Surrey. J. F. MACMAHON
A. D. B. CLARKE.

## CONSULTANTS IN DERMATOLOGY

SIR,—As a dermatologist who has also had charge of a venereal-disease department for over twenty-five years I fully endorse Dr. Ingram's protest (Nov. 26) that dermatological clinics should not be run by venereologists.

On the other hand I can see no reason why in certain instances V.D. clinics should not be undertaken by dermatologists. The work of the V.D. clinic, interesting and absorbing as it is, can be readily learnt by any competent consultant, and traditionally dermatologists have undertaken this work.

In sparsely populated areas it is surely more profitable for the dermatologist to move from the skin department to the V.D. clinic in one hospital than to waste his time travelling many miles to a distant hospital in order to undertake another dermatological clinic.

Dr. Campbell is wrong when he states (Dec. 17) that there are no young trainees qualified to practise both specialties adequately. All my own trainee dermatologists are given a thorough grounding in venereal diseases and have to work in the V.D. department. Those who have gone to some Commonwealth countries have found this training essential.

Finally, it should be noted that, whereas higher academic qualifications are required by consultants in dermatology, this is not the case in venereology.

London, W.1. JOHN L. FRANKLIN.

## ELECTRON-MICROSCOPY OF ATHEROMA

SIR,—Although in agreement with some of the findings reported by Dr. Levene (Dec. 10) we are in total disagreement over the material illustrated in figs. 5, 6, and 8, which we believe to be reticulin and *not* fibrin.

Electron-microscopic examination of the intima and inner aspect of media from normal fresh aorta and all the various stages of atheromatous formation (lipid streak, pearly plaque, chalky plaque, and ulcerating plaque) reveal a similar morphology consisting of the following components: (1) thick, dense fibres of elastic tissue; (2) large, irregular fenestrated elastic sheets; (3) very fine amorphous material; (4) striated fibres about 300–900Å in width, with a basic 220Å transverse banding with accentuation of each third component to give 640Å periodicity.

Numerous electron-micrographs demonstrate the intimate association of the fine amorphous material with these fibres to form the large, irregular sheets and thick dense fibres of elastin. Components 1, 2, and 3 have previously been demonstrated in aortic media.[1] It is significant that Dr. Levene does not mention the presence of typical elastic material. The striated fibres described under (4) are similar to those illustrated by Dr. Levene in figs. 5, 6, and 8. On the basis of their variable width and the underlying 220Å banding with accentuation of the 640Å periodicity, in our opinion they represent reticulin fibres as described by various workers.[2,3]

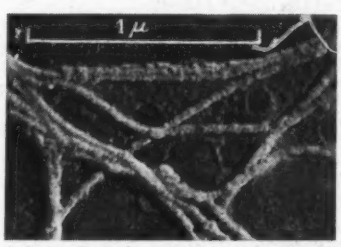
It is generally accepted that mature collagen is simply a closely compacted form of reticulin.[4–7] The fibres illustrated by Dr. Levene in figs. 5, 6, and 8, have a transverse periodicity of about 230Å and are closely similar to those found in maturing collagen. The amorphous material we found so closely associated with these fibres may well be the ultramicroscopic counterpart of the mucoid deposits described by Lindsay and Chaikoff[8] in naturally occurring aortic arteriosclerosis in the cat. These workers found that the initial histological lesion was accompanied by deposition of acid mucopolysaccharides in the intima which became gradually replaced by reticulum, collagen, and elastic fibres as the plaque matured.

We also feel that it is impossible to differentiate between fibrin fibres and those of reticulin and collagen by the action of tryptic enzymes on formalin-fixed material. In any case, Irving and Tomlin[2] have shown that unfixed samples of reticulin are susceptible to pancreatic digestion; the reticular argyrophilia is destroyed but may be restored by treating the fibres with either hyaluronic acid, blood plasma, serum, fibrinogen, albumin, or globulin.

Our own studies support Dr. Levene's observation that normal and pathological atheromatous intima give the same morphological picture. We consider, however, that the differences between the two conditions involves a preliminary disturbance of the collagen-elastin system rather than the deposition of fibrin which may occur later by encrusting the fully formed atheromatous plaques.

Leeds. M. K. KEECH
R. REED.

SIR,—With regard to Dr. Levene's paper I should like to mention that collagen may show a cross-banding with a periodicity of 210–220Å (i.e., a third of the usual 640Å periodicity), which makes it very difficult to distinguish between these fibrils and fibrin, especially since the exact magnification of the electron microscope cannot be gauged directly. This type of cross-banding is found in thin fibrils, which occur in tissues rich in mucoid—e.g., cornea (see accompanying figure).



Collagen fibrils from bull's cornea, showing 220Å cross-banding (× 35,000).

Microbiological Laboratory, University of Amsterdam. A. VAN DEN HOOFF.

## HEROIN

SIR,—In an annotation on Dec. 3 you advocated the abolition of the use of heroin by the profession in an article which was remarkable for its lack of balance. It appeared to be written from an editorial chair which knew little of the practical use of heroin. You stated that "The Royal Colleges, the British Medical Association, or the whole profession through a plebiscite, could . . . have expressed an opinion." May I draw your attention to the fact that the whole profession has expressed its opinion in a most emphatic manner, and has strongly protested against the ban on heroin:

1. At the Annual Representative Meeting of the B.M.A. held on June 3 last there were about 450 delegates present who represented all the B.M.A. divisions and branches in this country. They came armed with a mandate from their constituents and by a large majority the following motions were passed:

"That this meeting protests against the threatened withdrawal of the most excellent sedative heroin which is of inestimable value in so many conditions, and recommends that it should still be manufactured in this country for use by medical practitioners but not exported."

1. Hall, D. A., Reed, R., Tunbridge, R. E. *Exp. Cell Res.* 1955, 8, 35.
2. Irving, E. A., Tomlin, S. G. *Proc. roy. Soc.* B. 1954, **142**, 113.
3. Robb-Smith, A. H. T. *In* Connective Tissues: Transactions of the 3rd Conference, Josiah Macy, jun., Foundation. New York, 1952; p. 92.
4. Wyckoff, R. W. G. Electron Microscopy. New York, 1949.
5. Wyckoff, R. W. G. *In* Connective Tissues: Transactions of the 3rd Conference, Josiah Macy, jun., Foundation. New York, 1952; p. 38.
6. Vanamee, P., Porter, K. R. *J. exp. Med.* 1951, **94**, 255.
7. Burton, D., Reed, R. *J. Soc. Leath. Tr. Chem.* 1953, **36**, 13.
8. Lindsay, S., Chaikoff, I. L. *Arch. Path.* (*Lab. Med.*) 1955, **60**, 29.

"That the meeting instructs Council to seek direct access to the Government to obtain the reversal of the decision on the banning of heroin."

2. The medical committees of eleven out of twelve undergraduate teaching hospitals in London (representing over 500 consultants) sent a letter to the Minister of Health protesting against the heroin ban. A number of medical committees of postgraduate teaching hospitals in London did likewise.

As the matter is sub judice by the Government it is important that this overwhelming verdict of the profession should be given the greatest prominence.

London, N.W.1. E. C. WARNER.

## INDOLE DERIVATIVES

SIR,—In your leading article on argentaffinoma (Nov. 12) you hinted at a possible connection between 5-hydroxytryptamine (serotonin) and plant-growth hormones.

After Friedman et al.[1 2] had found that the urine of patients with chronic myeloid leukæmia contained indirubin (double indole-derivative) in higher concentrations than normal, I investigated the effect of indirubin and also of plant-growth hormones on the white blood-cell count in the guineapig. Indirubin causes a transitory leucopenia; plant-growth hormones cause neutrophil leucocytosis and increase in eosinophils. Plant-growth inhibitors have the reverse effect.[3]

Like you, I believe that indole derivatives may have special effects in warm-blooded animals. Further investigation of indole derivatives in connection with the white blood-cells might be of interest.

Interne Kliniek,
Rijksuniversiteit,
Ghent, Belgium. B. C. DE LANDSHEERE.

## PREDNISONE AND PREDNISOLONE IN RHEUMATOID ARTHRITIS

SIR,—I read with interest the paper by Dr. Dudley Hart and his colleagues (Nov. 12) in which they record their results with prednisone and prednisolone in the treatment of 14 patients with rheumatoid arthritis. I would like to add my experience with prednisolone.

18 patients with very severe rheumatoid arthritis were chosen for this preliminary trial from a large number attending an outpatient clinic whose previous therapy had not proved entirely satisfactory. 3 had been treated with aspirin or allied drugs, 10 with phenylbutazone (by mouth in 3 cases and by intramuscular injection in 7), and 5 with cortisone. All the patients who received cortisone had been unsatisfactorily treated with phenylbutazone by mouth and by injection. The beneficial effect of the prednisolone was assessed by noting the improvement in the pain, stiffness, and tenderness in the joints. Any reduction in the swelling and increase in the range of the movements of the joints was also taken into consideration. The improvement reached its maximum within two days after starting administration of 5 mg. of prednisolone four times a day, and the majority were subsequently satisfactorily maintained when the dose was reduced to 5 mg. twice a day. All the patients remained for one week in hospital and after discharge have been followed up in an outpatient department at three-weekly intervals, for two to three months. 2 relapsed but subsequently regained their improvement when the dose was increased to 5 mg. three times a day. No toxic side-effects have been observed.

The results of this short-term trial indicate that prednisolone is much more effective than cortisone in relieving the symptoms and signs of rheumatoid arthritis. In most cases the dose was a quarter that prescribed with cortisone. In this respect my results agree with those of Dr. Dudley Hart and his colleagues, but they differ slightly in that all my patients preferred prednisolone to cortisone whereas 5 of their patients were indifferent.

Prednisolone, judged from the results in this small series of cases, is more effective than any previous drug in the control of the signs and symptoms of rheumatoid arthritis.

In addition prednisolone has had a beneficial action in the control of a case of severe hæmolytic anæmia, and relieved a patient with giant urticaria who was completely resistant to all other forms of therapy.

Prednisolone was supplied for trial as 'Meticortelone' by the Schering Corporation, and as 'Delta-Cortril' by Messrs. Pfizer Ltd.

Dudley Road Hospital,
Birmingham. R. O. GILLHESPY.

## INSTITUTIONALISATION

SIR,—Your challenge (Dec. 17, p. 1301) must not be allowed to pass unanswered. Anyone on consideration could, without importing Civil Service jargon, suggest half a dozen suitable titles for the article in question, for the English language is singularly rich in words of one or two syllables.

I could not attempt to suggest any word or words "with the same signification" (significance?), for I do not know what the word means: I doubt very much if any of your readers do either. If you yourself cannot define it in simpler terms, you would appear to be guilty of printing meaningless gibberish.

We all admire *The Lancet* as a literary, as well as a medical, journal. I hope that it will long continue to be so, and that you will resist the use of ugly, unnecessary, and indefinable words.

Newcastle upon Tyne. M. H. ARMSTRONG DAVISON.

SIR,—Though Dr. Armstrong Davison protests against the word institutionalisation he will probably be glad to hear that the process of disinstitutionalisationism is taking place in his own region.

The need for it may be judged by the response of a mentally defective hospital patient who, when taken on a Christmas shopping expedition to an erstwhile sixpenny store, exclaimed: "By——what a smashing sale-of-work."

Northgate and District Hospital,
Morpeth, Northumberland. C. GUY MILLMAN.

## POLIOMYELITIS

SIR,—In view of the previous letters by Dr. Breen and Dr. McMath (Oct. 29) and Dr. Laurent (Nov. 19) with their reports on the cerebrospinal-fluid (C.S.F.) findings in recent outbreaks of poliomyelitis, our experience in this regard at Stoke Mandeville Hospital may be of interest.

In the period from July 24 to Dec. 1, 1955, 58 cases of poliomyelitis (18 non-paralytic and 40 paralytic) were admitted to the unit directed by Dr. W. Ritchie Russell. The C.S.F. was examined early in 17 of the 18 non-paralytic and in 14 of the 40 paralytic cases; and, as the accompanying table shows, there was no significant difference between the findings in the two groups.

C.S.F. FINDINGS IN POLIOMYELITIS

| — | Paralytic (14 cases) | Non-paralytic (17 cases) |
|---|---|---|
| *Duration (days) of major illness before C.S.F. examination:* | | |
| Average | 3·2 | 3·36 |
| Range | 1–6 | 1–6 |
| *Total white blood-cells (per c.mm.):* | | |
| Average | 87 | 94 |
| Range | 2–184 | 0–389 |
| *Polymorphs:* | | |
| Average per c.mm. | 40 | 66 |
| Range per c.mm. | 2–117 | 0–350 |
| Average % of total | 52 | 58 |
| Range % of total | 5–100 | 0–97 |
| *Protein (mg. per 100 ml.):* | | |
| Average | 56·1 | 55·7 |
| Range | 30–110 | 18–170 |

1. Friedman, E., Jacobson, W. *Nature, Lond.* 1946, **157**, 337.
2. Friedman, E., Marrian, D. H., Perutz, M. F. *Biochim. biophys. Acta*, 1950, **5**, 75.
3. de Landsheere, B. C. *Experientia*, 1951, **7**, 307; *Arch. int. Pharmacodyn*, 1952, **90**, 363; *Ibid*, 1953, **94**, 365.

The high polymorph counts found during the early stages in both groups are similar to those recorded in many other outbreaks. In fact the proportion of polymorphs was over 50% in 8 of the 14 paralytic, and in 12 of the 17 non-paralytic cases. (In another case recently admitted to the respiration unit in Oxford, the C.S.F., examined a few hours before paralysis appeared, contained 1020 cells per c.mm., of which 96% were polymorphs.)

Like your other correspondents we have not had the benefit of help from virus laboratories during this sharp outbreak.

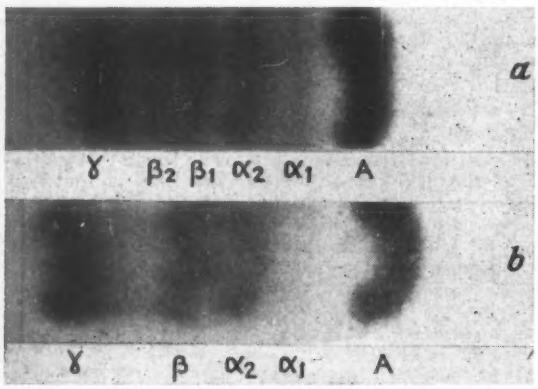
Department of Neurology (United Oxford Hospitals), Stoke Mandeville Hospital, Aylesbury, Bucks.

J. DOMINIAN
M. L. E. ESPIR.

## ELECTROPHORESIS OF PLASMA-PROTEINS

SIR,—In his letter of June 11, Dr. Christiansen reports splitting of the β-globulin band in serum from some patients in the fasting state after heparin injection. He observes that no separation occurred when heparin was given after a fatty meal.

We have found recently, however, in the course of some experiments on the clearing mechanism of heparin,




**Electrophoresis of serum during alimentary lipæmia (*a*) before and (*b*) after injection of heparin.**

that the splitting of the β-globulin band occurred in 2 cases during alimentary lipæmia *before* the administration of heparin; 30 minutes after intravenous injection of heparin the splitting disappeared in the "cleared" serum. This is, however, a rare phenomenon: in 35 other cases we failed to observe this splitting after the fatty meal, although the electrophoresis took place under the same conditions. The absence of splitting in the fasting state and the disappearance after the administration of heparin support the hypothesis that splitting may be caused by some change in the lipoprotein pattern of the serum.

S. GERÖ
M. JAKAB
M. BAUMAN
S. ROHNY
J. GÁCS.

III. Medical Clinic, University of Budapest.

## HYDROCORTISONE IN PAINFUL SHOULDER

SIR,—Mr. Waugh (Nov. 5) must not think that my methods of examination fail to take account of pain referred to the shoulder, not only from the neck and thoracic outlet, but from the arm and forearm as well.

In the article on hydrocortisone that Dr. Troisier and I wrote in 1953,[1] we devoted a quarter of the space to clinical examination; for that alone shows where the injection must be given.

1. Cyriax, J., Troisier, O. *Brit. med. J.* 1953, ii, 966.

I have always emphasised that the entire segment within which a pain arises must be examined. In the case of the shoulder this involves examination of the neck, scapula, shoulder, elbow, wrist, and fingers. If Mr. Waugh will look at my *Textbook of Orthopædic Medicine* (1954), he will find that I divide the examination of the shoulder into two parts. Stage 1 (p. 219) describes the preliminary examination that determines whether or not the shoulder area contains the lesion. If this proves so, detailed examination of the tissues at the shoulder follows (pp. 220–236).

London, W.1. JAMES CYRIAX.

## MORPHINE ANTAGONISTS

SIR,—I read with interest the observations by Dr. Bonnycastle and Dr. Costa (Sept. 10) concerning the actions of bemegride (ββ-methyl-ethyl glutarimide, 'NP13,' 'Megimide') and amiphenazole (2:4-diamino-5-phenyl thiazole hydrochloride, 'DAPT,' 'Daptazole,' 'DHA245') given either individually or in combination as antagonists to opiate-induced or barbiturate-induced respiratory depression in rats.

Results of experiments with these drugs appear to indicate that the rat responds less like man than does the dog. The dog has been awakened under electro-encephalographic control[1] from morphine or light barbiturate narcosis by the gradual administration of amiphenazole alone, or from deep barbiturate narcosis with a mixture of amiphenazole and bemegride, without producing any clinical or electro-encephalographic signs of incipient convulsions. There further appeared to be an increase in respiratory activity before the animals awoke. However, respiratory minute-volume was not measured. When these drugs—especially bemegride—were administered more rapidly and in larger doses convulsions were produced which rapidly subsided. We have deliberately induced convulsions several times in a single experiment without the loss of an animal.

Preliminary experiments in collaboration with E. R. Trethewie on the decerebrate cat indicate that amiphenazole will increase the respiratory minute-volume. This increase is not wholly accounted for by any generalised movements (which indeed may be absent) indicative of increased motor activity. A similar dose of amiphenazole administered to the intact cat has produced no signs of increased motor activity.

Comparison with niketamide suggests that amiphenazole is at least as effective dose for dose in increasing respiratory ventilation. Bemegride, however, does produce signs of increased motor activity in doses which promote respiratory stimulation.

Although not denying that in excessive doses these drugs have a central stimulant action we maintain that, if administered as advised in the treatment of barbiturate intoxication or morphine depression, they have a wide margin of safety. In regard to the reported signs of toxicity after the administration of bemegride[2] or amiphenazole,[3] these were observed in our earliest cases and were due to too rapid administration and excessive dosage, through lack of experience. We have since had no cause for concern, but one should always be on the lookout for the occasional, perplexing case of idiosyncrasy.

Finally I wish to refer to the high therapeutic safety of amiphenazole.[4]

1. Amiphenazole has been administered intravenously in divided doses over 20–30 minutes to 17 young healthy unnarcotised volunteers in doses of up to 225 mg. without producing any acute or residual symptoms or signs of toxicity. As much as 60–90 mg. was given in one dose on 12 separate occasions.

2. Amiphenazole has been given to a critically ill patient with congestive cardiac failure, bronchopneumonia, and post-operative shock following repair of a ruptured gastric ulcer. A dose of 15 mg. was administered half-hourly (720 mg. per

1. Shaw, F. H., Simon, S. E., Cass, N. M., Shulman, A., Anstee, J. R., Nelson, E. R. *Nature, Lond.* 1954, **174**, 402.
2. Shulman, A., Shaw, F. H., Cass, N. M., Whyte, H. M. *Brit. med. J.* 1955, i, 1238.
3. Shaw, F. H., Shulman, A. *Ibid*, p. 1367.
4. Shulman, A. Unpublished.

day) as a buffer to a depressed respiration. This treatment was continued for 14 days until the patient died, without any obvious symptoms or signs suggesting drug toxicity. At necropsy low-grade peritonitis was found which was due to silent rupture of the suture-line.

Although amiphenazole has not been effective in every case, its clinical value should be fully investigated in view of its safety in therapeutic doses (5–50 mg.).

I thank Mr. C. D. Donald, honorary inpatient surgeon, and Dr. L. C. Hudson, medical superintendent, Prince Henry Hospital, Melbourne, for permitting me to refer to this case, which was under their care.

Physiology Department, University of Melbourne. A. SHULMAN.

# Obituary

## THOMAS BENJAMIN DAVIE

B.A. Stellenbosch, M.D. Lpool, LL.D. Camb., F.R.C.P., F.R.S.S. Afr.

Professor Davie came to this country last month to represent, as its principal and vice-chancellor, the University of Cape Town at the Queen Mother's installation as Chancellor of the University of London. While he was in this country his own University of Liverpool and the University of Oxford had hoped to give him honorary degrees. But owing to his illness the ceremonies had to be postponed, and he died in London on Dec. 14. These academic honours were his colleagues' recognition of the leadership which he had offered during seven difficult years to the vice-chancellors of the Commonwealth. In conference he consistently urged that universities must stand for academic freedom independent of race, creed, or colour, and by his own courage he set an example of how to say No to governments which would make universities a tool of politics.

[*Liverpool Daily Post*

He was born in 1895 in South Africa and he graduated B.A. in 1914 at the University of Stellenbosch. In 1917 he joined the Royal Flying Corps and was completing his training as a pilot officer at the time of the Armistice. After demobilisation he returned to South Africa, where he taught science in several boys' schools. In the early part of 1922 he served with the Transvaal Scottish Regiment during the rebellion which broke out in Johannesburg in that year. A bullet wound in his thigh left him with slight permanent shortening of a leg.

Two years later he came to this country to study medicine at Liverpool University, where he graduated M.B. with first-class honours in 1928. A colleague who first met him while he was holding house-appointments at the Liverpool Royal Infirmary describes him as "noticeable among the residents by his greater age, maturity, and physique. Davie stood head and shoulders, physically and in personality, above his medical generation in Liverpool. As might be expected, he had played a great part in student activities, writing for the annual medical dinner songs which were largely based on Gilbert and Sullivan and which were always sung with great zest."

While still a student he had held the Holt fellowship in physiology, and during his tenure he did much of the work on the production of antibodies on which was based the thesis for which he was awarded his M.D. in 1931. Meanwhile, in 1929, he had been appointed to the junior lectureship in pathology at the University of Liverpool under Prof. J. H. Dible. In 1931 he was appointed pathologist to Walton Hospital, where he reorganised the pathological service. While he was at the hospital he maintained his contacts with the university, and in 1933 he returned to the department of pathology as senior lecturer. He was a gifted and energetic teacher, combining schoolmasterly didacticism with a light and bantering method of questioning. His famous Saturday morning class on the accumulated specimens of the week, with its cut and thrust, question and repartee, became a feature in the medical school. In 1935 he was appointed to the chair of pathology in the University of Bristol. Three years later he succeeded Professor Dible at Liverpool. In 1940 he was elected F.R.C.P.

The outbreak of war in 1939 revealed his talent for administration. He organised the first blood-bank in Liverpool and soon was taking part in the arrangements for a pathological service over a large part of the North of England, in active collaboration with the Ministry of Health and the Emergency Medical Service. During the blitz on the Western Approaches his service faced grim weeks of bombing. A colleague recalls his voice "cheerful and gay as usual" coming over the telephone one morning to say "that the whole of his transfusion service had been blown up—autoclaves and everything—could we send what we had?"

He was also continuously and widely immersed in the inner affairs of the medical school and university, and in 1946 he became whole-time dean and began to give more and more time to administration. His ability was quickly recognised and in 1947 he was invited to return to South Africa as principal and vice-chancellor of the University of Cape Town. He was thus appointed to a difficult job at a difficult time, and almost from the moment of his arrival he was handicapped by a sudden and disabling attack of rheumatoid arthritis which permanently crippled him. The policy of apartheid fell heavily on Cape Town University, which is one of the two South African universities which admits students irrespective of race or colour. In maintaining this traditional academic freedom Davie was both firm and statesmanlike. He remained simple and friendly but also firm, never weakening in his belief that a university should be "universal." As he himself put it earlier this year in the Hoernlé memorial lecture: "Its doors should at all times be open to everyone who can benefit by or contribute to its teaching. Its desire for freedom from interference is primarily directed to what is taught, but is inextricably bound up also with who shall teach and who shall be taught."

J. H. D., who was closely associated with him in his early years at Liverpool, writes: "Tom Davie was a big man in many ways; physically and morally. He was forthright, good humoured, genial and withal strong. He was not a man to be upset by difficulties. They seemed to fade away and be blown out of existence before his good-humoured bulk and breezy manner. He was a fighter for any cause he believed in, but always a chivalrous and worthy opponent. He enjoyed life, he enjoyed being in the swim, and he enjoyed doing things. He did well and, as the minister said at his funeral—and the words rang true in the memories of those who knew him—'he was steadfast to the end.'"

Dr. Davie married in 1921 Vera C. Roper, who survives him. There were no children of the marriage.

## LIONEL VERNON CARGILL

F.R.C.S.

Mr. Cargill, consulting ophthalmic surgeon to King's College Hospital and consulting surgeon to the Royal Eye Hospital, died on Dec. 13 at the age of 89.

He was educated at King's College School, and in 1894, with a Salter's university exhibition, he entered the medical department of King's College. He continued to win many of the prizes and scholarships available, including the Sambrooke exhibition, and after he had passed the intermediate M.B. examination he was appointed assistant demonstrator in physiology at King's College. In his final years he continued to carry off many awards, and in 1889 he was senior scholar of his year and received Sir Joseph Lister's clinical surgery prize. After qualifying in 1890, he was almost immedi-

ately appointed ophthalmic clinical assistant to Prof. M. M. McHardy, who confirmed Cargill's decision to specialise in ophthalmology; but he also held the post of house-surgeon to Lister.

In 1892 he took the F.R.C.S. and became the first house-surgeon and surgical registrar at the Royal Eye Hospital, where for some time he had already been a clinical assistant. Two years later he was appointed Sambrooke surgical registrar at King's. In 1894 he joined the honorary staff of the Royal Eye Hospital and in 1899 he was elected assistant ophthalmic surgeon to King's. He was now well launched on his career and his private practice grew. But he found time to serve on the staff of the Seamen's Hospital, Greenwich, perhaps partly because of his interest in the Thames estuary, where he spent many congenial weekends on his yacht.

During the Boer War he went to South Africa as ophthalmic surgeon to the Imperial Yeomanry Hospital, and in the 1914–18 war he was consultant for diseases of the eye in military hospitals in London and had charge of the ophthalmic beds at the 4th London General Hospital.

In 1931 he retired from the staff at King's and in the same year he was elected chairman of the council of the Royal Free Hospital. He also became a member of the court of the Society of Apothecaries, which in 1890 had granted him his first medical qualification, and in 1939 was master. In the same year he was appointed a fellow of King's College.

Mr. Cargill's wife died four years ago. He leaves three daughters.

## CHARLES HENRY ALLEN

O.B.E., M.B. Edin., F.R.C.S.E.

Mr. C. H. Allen died on Dec. 10 at the age of 78, in the General Hospital, Nottingham, to which he had given many years of service as honorary surgeon.

A farmer's son from Metheringham in Lincolnshire, he was a student at Edinburgh University where he graduated M.B. in 1900. The same year he went to the Nottingham General Hospital as assistant house-surgeon, and after obtaining the F.R.C.S.E. in 1906 he was appointed to the honorary staff in 1907.

In his early days he was an active Territorial officer, and at the outbreak of the 1914–18 war he was a captain in the 3rd North Midland Mounted Brigade field ambulance. In the spring of 1915 he went to Egypt with the brigade, and he was later detached from the field ambulance to command Ras-el-Tin Military Hospital. He was three times mentioned in despatches for his services in the field, twice by Lord Allenby, and later he was appointed O.B.E. and awarded the Order of the Nile (4th class).

After the war he returned to his work as honorary surgeon at the General Hospital, Nottingham. He was also for many years consultant surgeon to the City Hospital. He was a fellow of the Association of Surgeons, and in 1931–32 president of the Nottingham Medico-Chirurgical Society. Later he became senior surgeon and chairman of the medical committee of the hospital. He retired from consultant practice in 1946, after being requested by the hospital board to continue his work as a surgeon during the war for four years past the retiring age.

J. F. S. writes: "C. H., as he was called by all of us at the General, had a shrewd clinical sense and was essentially a safe surgeon. Conscientious to a high degree, he did not stint himself in the care he gave to his patients; the more ill the patient, the harder he fought. He had an informed mind on many subjects and could be a most entertaining companion with a lively sense of humour. He spoke little of his own attainments. He was keenly interested in sport; his favourite recreation was hunting and he especially loved a good horse. For many years he was a prominent member and follower of the Blankney Hunt in Lincolnshire. He was also an enthusiastic, though indifferent, golfer, and he was widely read on the game, as he was on all subjects in which he took an interest, and this applied in even greater measure to his chosen profession. He was a staunch friend and will be well remembered by his own colleagues and his wide circle of friends."

## EDWARD AULT MARSON

M.B. Manc., F.F.A. R.C.S., D.A.

Dr. Marson, anæsthetist to the Manchester Royal Infirmary, died on Dec. 8 at the age of 55.

He was educated at Hulme Grammar School and Manchester University where he graduated M.B. in 1925. After holding resident appointments at Ancoats and St. Mary's Hospitals, he set up in general practice in Manchester. It was not long before he became a visiting anæsthetist to Ancoats Hospital and Stockport Infirmary. His anæsthetics practice increased so much that in 1937 he gave up his general practice to give all his time to anæsthetics. In 1949 he was appointed to the staff of the Manchester Royal Infirmary as a consultant anæsthetist.

Though of a modest and unassuming nature, Marson did much to forward the local development of his specialty. He was one of the prime movers in the formation of the Manchester and District Society of Anæsthetists in 1945 and he was the first honorary secretary. After the society amalgamated with the Manchester Medical Society, he was in 1952 elected president of the section of anæsthetics.

C. E. S. writes: "Marson would answer a call for help from a colleague with a generous expenditure of time and energy. His gentle care and consideration for his patients was boundless and to those with whom he worked he was courteous, patient, and understanding. During the last few years he was often gravely ill, but he carried on cheerfully and with no word of complaint. His example is an inspiration to us all."

Dr. Marson leaves a widow and a daughter.

## Prof. P. A. BUXTON

Sir Philip Manson-Bahr writes:

"Seldom, since the days of Darwin and Wallace, has there been such a competent and all-round naturalist as Patrick Buxton. He had great accomplishments, a vivid active brain, great powers of observation, an innate love of Nature, and a great talent in description. His literary style was impeccable, and he was a witty and exceptionally good speaker. It is not generally known how widespread were his interests. Besides being a field naturalist, he was a good ornithologist with several new species to his credit, and he was a first-rate botanist and a good gardener. His monographs are models of their kind, and are replete with all manner of data which he was able to correlate in a remarkable manner. In them he appears as an expert on meteorology, history, geology, and kindred sciences which he welded into a complete whole. His greatest work is his magnificent *The Natural History of Tsetse Flies* published in 1955. By reason of little personal peculiarities and mannerisms a host of stories grew up about 'Buggy Buxton,' as he was affectionately called. He usually wore a rare flower or leaf in his buttonhole and was never so happy as when giving away rare plants out of his garden to his friends."

Prof. V. B. Wigglesworth writes:

"When Buxton was appointed head of the department of medical entomology at the London School of Hygiene and Tropical Medicine in 1926, he realised that the development of medical entomology was being impeded by lack of knowledge of the physiology of insects, and I was the first of a long series of research workers whom he recruited to this field. I remained in his department for nineteen years and I found him an admirable chief. For I am only one among folk who are now scattered all over the world who benefited from Buxton's thoughtfulness for others. His very characteristic manner, with some element of display, and a large element of sarcasm, could be amusing or irritating—but those who knew him best were so well aware of the true quality of the man that they learned to disregard this protective mannerism. In his last few years, in devoting himself to the tsetse-fly problem on the widest front, Buxton was able to exhibit to the full his great talents as a naturalist. He was also developing with enthusiasm a new field of natural-history study for his coming years of retirement and, mellowing with the years, the veneer of his manner wore off and revealed for all to see the kindness, honesty, and unselfishness which made up a great character."

## Professor EGAS MONIZ

Sir Geoffrey Jefferson writes:

In spite of the gout which had so much interfered with his hands and with his mobility for some years past, Professor Egas Moniz remained as alert intellectually and as interested as at any time, so it seemed at the time of the Fifth International Congress of Neurology held in Lisbon under his presidency in 1953. His famous hospitality and his friendliness were undiminished. One of his last publications was his beautifully reproduced history of playing-cards, *Tratado do jogo do Boston*, 1952.

His life, now that it has come to its end, can be seen in perspective, and the impression that it gives is that it was a happy and unusually productive one. His name will live for his two great contributions to medicine. Because both of these innovations were of a surgical nature, Professor Egas Moniz has often been referred to as a neurosurgeon. This he was not. Dr. (now Professor) Almeida Lima had usually acted as his surgical hands. He was not only professor of neurology in Lisbon but, by training, a neurologist of the Paris school, a close friend of Babinski and, like Babinski's brother, a gourmet. Certainly he looked to Paris always for its approval, it was before the French neurologists that he preferred to test his ideas. His first tentatives in angiography were given at a meeting of the Société de Neurologie de Paris in 1927 and his first 20 cases of prefrontal leucotomy were reported to the Académie de Médecine in 1935.

Babinski in the preface which he wrote not long before he died to Egas Moniz's book in which the value of angiography was first massively demonstrated (*Diagnostic des tumeurs cérébrales*, Paris 1931) quoted Paul Valéry. Valéry had said that scientific discovery is less important, or less interesting perhaps, because of what follows from it than is the analysis of the intellectual processes which brought it to birth. This was a very apt quotation. No-one who was privileged to watch the development of Egas Moniz's discoveries could help but admire the ways in which they were developed. He turned to angiography because he was dissatisfied with the limitations of neurology alone in brain-tumour localisation and especially its failure to distinguish between one kind and another. Although very many thousand angiograms have now been made, Egas Moniz, with the assistance of Almeida Lima, had already in 1931 observed and recorded all the basic facts—the bilateral filling obtained when one carotid is compressed, the elevation of the pericallosal vessels in hydrocephalus, as well as the displacements of vessels and tumour fillings which, though now commonplace, were twenty-five years ago exciting exhibits. Furthermore, he, Almeida Lima, and Rui de Lacerda had in 1931 shown the first arteriographically proven cases of carotid thrombosis, a subject that Egas Moniz returned to in 1940 and 1947.

To the general public Professor Egas Moniz was better known no doubt because of prefrontal leucotomy, an operation first really popularised in Britain by Wilfred Willway at Bristol with Professor Golla's encouragement. Egas Moniz told how he was led to leucotomy through the description by John Fulton and Jacobsen of the disappearance of anxiety behaviour and temper tantrums in monkeys after bilateral frontal ablations. He illustrated here better than in angiography Paul Valéry's dictum. The Nobel prize which he shared with W. Hess of Zürich was the fitting crown. Looking back, it is clear that just as many thought that Walter Dandy's introduction of pneumography was more important than anything that Harvey Cushing did (which is one of those truths which are mainly wrong) so Professor Egas Moniz overtopped Dandy. Humanity has reason to pay its last respects and express its gratitude to another very great Portuguese explorer. The fullness of that personality can only wholly be appreciated by those informed of his complete history from his early political days when he led the Portuguese delegation to the peace conference after World War I.

Those of us who knew Egas Moniz personally and his charming wife will regret greatly that so intelligent, so humane, and so charming a personality has gone from amongst us.

# Births, Marriages, and Deaths

## DEATHS

MONTGOMERY.—On Dec. 13, at the Royal Northern Hospital, London, James Aitken Montgomery, M.D., physician-superintendent, Coppetts Wood Hospital, London.

# Notes and News

## STAFFING A KOREAN HOSPITAL

SOME two years ago the Society of Friends sent a team to Kunsan, a port on the west coast of Korea, to help in restoring the work of the civilian hospital there. Unlike the mission hospitals organised on Western lines, Kunsan Hospital has retained much of its Korean character, with a Korean medical superintendent and staff; but American and British doctors and nurses have contributed modern Western knowledge and experience in treatment.

At the time of the team's arrival Korean doctors had been out of touch with modern medical practice for many years; but, with the aid of their Western colleagues, they have been able to provide medical care of a good standard. In this they have been greatly helped by the visits, lasting three months, of a physician who gave a series of lectures and ward rounds, and of a surgeon who demonstrated surgical techniques which Korean doctors were later able to practise. Full training programmes for nurses and laboratory technicians have also been arranged. At present, 70% of the patients in the hospital are "on relief" and are non-paying. In accordance with Korean custom, patients' relations help with their treatment and cook their meals; there is a central kitchen to provide meals for those patients who have no-one to cook for them.

It is hoped that the hospital will be well staffed and running efficiently by the time it is transferred completely to the Koreans in two years' time. Much, however, remains to be done and the Society of Friends are anxious to find a doctor who is prepared to go to Kunsan Hospital for a period of eighteen months. The services of a physician who will continue the teaching for a period of three months would also be welcome.

Inquiries about this valuable and rewarding work should be addressed to Lewis E. Waddilove, Beverley House, Shipton Road, York.

## NEW OCCUPATION CENTRE IN LEEDS FOR MENTALLY HANDICAPPED

ON Nov. 29 Dr. G. E. Godber, deputy chief medical officer of the Ministry of Health, opened a new occupational centre for mentally handicapped children in Leeds. Leeds now has five centres catering for 453 people, and the new centre will take 108 children under sixteen. It has been designed by the city architect, and the cost of the building was £44,000. It contains a large combined dining and assembly hall, administrative rooms, and nine class-room blocks set at right-angles to the assembly hall. In opening the new centre Dr. Godber said that Leeds has led the world in the care of the mentally handicapped. Dr. Z. P. Fernandez, chairman of the mental health services subcommittee of the city council, said that Leeds spent more in this field than any other local authority in the country, averaging £103 per thousand of population as against £7 or £8 in other areas. The city had the highest ascertainment record in the country and in his experience incorrect certification was unknown.

### University of London

The title of reader in biochemistry has been conferred on Mr. A. L. Greenbaum, PH.D., in respect of his post at University College.

### University of Durham

On Dec. 17 the degrees of M.B., B.S. were conferred on the following:

J. W. Alderson, J. P. R. Campbell, * P. N. Cowen, Dorothy M. H. Dickinson, Kathleen H. Fowler, B. R. Hayes, Sylvia J. Jayson, * D. M. H. Jones, Veronica Marr, M. B. Mummery, T. C. Nelson-Williams, J. O. Odulate, Wahab Olabode Oshodi, D. L. Pearson, G. A. Turnbull, Sheila M. Waterhouse, J. C. White, Jean C. Whitfield.

* In absentia.

### University of Bristol

On Dec. 19 degrees of M.B., CH.B. were conferred on the following:

Aboyomi Babbatunde Claudius-Cole, M. R. Clift, Izette R. Coulton, Arummugam Ganendran, J. A. Hayes, W. G. R. Hobbs, D. I. D. Hodge, I. M. Joiner, F. J. M. Killick, Stella A. F. Maxted, Margaret E. C. Parke, R. P. Saundby, D. W. Seldon, J. A. C. Strachan, M. T. White, J. H. Williams.

### University of Manchester

The following have passed the final examination for the degrees of M.B., CH.B. :

James Adams, E. S. Ainsworth, Norman Beenstock, J. N. Bowers, E. C. Cockings, R. P. Davis, A. W. Drummond, T. B. Edwards, Anne E. Evans, Joseph Glass, S. L. Goodman, Audrey W. Gostling, C. A. A. Haigh, Catherine E. Hall, Susan Hetherington, J. N. MacCaig, Anne Maclachlan, J. G. M. Maclachlan, J. D. Mason, Brian Peach, Sheila G. Quain, Gillian P. Roach, Raine E. I. Roberts, J. H. M. Robertson, Eric Rowley, Beryl Sephton, Anne E. Treharne.

### University of Liverpool

At recent examinations the following were successful :

*M.D.*—F. G. Anderson, Cynthia J. Discombe, R. J. Fallon, W. L. Sanders, J. K. Wilson.

*M.Ch. Orth.*—M. Alms, Sheroo D. Bharucha, P. G. Brady, J. H. C. Carrier, H. S. Y. Fang, P. Kilburn, H. Klein, I. L. Macfarlane, I. K. Sharp, G. C. Slee, H. Thompson.

*M.B., Ch.B.*—J. R. Burrows, W. Caplan, Mary R. Daniel, P. W. Davies, M. M. Gerassimos, R. G. Ingham, Audrey E. Jaques, C. D. Krasner, E. Lewis, G. S. Wilson, E. M. W. Wong.

### University of Birmingham

On Dec. 16 the following degrees were conferred :

*M.D.*—C. G. Berry, D. L. Crombie.

*Ch.M.*—J. A. Mantle.

*M.B., Ch.B.*—Eric Anthony, George Atkins, J. E. Backhouse, Brian Baker, John Bennett, J. A. Binnie, A. H. Brittain, Brenda M. Browne, Nancy G. Campbell, R. H. Cawley, M. J. Daly, J. B. Davies, H. R. Dobson, J. D. Earp, R. I. Froment, Harrydewa Goriah, Daphne E. Mahabir, M. E. T. D. R. Maigrot, Stanley Middleburgh, D. W. Millard, Helen W. Rogers, M. G. Saunders, L. W. Smith, M. P. Taylor.

### University of Sheffield

Dr. S. K. R. Clarke has been appointed lecturer in bacteriology and virus diseases.

### University of Edinburgh

On Dec. 16 the following degrees and diplomas were conferred :

*M.D.*—Margery A. Lawley, *J. A. H. Lee, *Rachel B. Mackay (with honours), D. S. McLaren, J. B. Primmer, *J. D. Robertson, J. L. Stewart.

* Commended for thesis.

*D.Sc.*—G. W. A. Dick.

*Ph.D. (in the faculty of medicine).*—G. D. Forwell.

*M.B., Ch.B.*—Catherine G. Butcher, C. S. Cairns, I. M. Campbell, R. I. Davies, T. K. Hay, I. M. Hourston, J. O. Jones, Thalia H. Lowe, R. T. McKay, J. C. Ramsay, M. D. Scott, P. M. Shaw, J. R. M. Shepherd, Isobel M. Sinclair, Phyllis Watson, Evan Whittaker.

*D.P.H.*—Ariane G. M. Wiseman.

*D.M.R.D.*—J. K. Davidson, Lockhart Frain-Bell, K. W. M. Grossart, M. W. M. Hadley, Hamish Innes.

*D.M.R.T.*—J. T. Lamb, A. L. Meikle, William Muirhead.

*D.Psychiat.*—Frank Badrock, P. G. McGrath, H. B. Milne.

### Royal College of Physicians of London

On Tuesday, Jan. 10, Dr. R. T. Brain will deliver the Watson Smith lecture. His subject will be the Clinical Vagaries of the Herpes Virus. The first Marc Daniels lecture will be given by Sir Geoffrey Todd on Thursday, Jan. 12. He is to speak on Chemotherapeutic Control in the Treatment of Fibro-nodular Pulmonary Tuberculosis. Both lectures will be given at 5 P.M. at the college, Pall Mall East, S.W.1.

### Royal College of Surgeons of Edinburgh

At a meeting of the college held on Dec. 14, with Prof. Walter Mercer, the president, in the chair, the following were admitted to the fellowship :

Jayalakshmi Yegnanarayan Ayer, Shyam Kishinchand Bulchandani, Remo Cantamessa, George Fahmy, N. P. G. Fischer Kizhakevettil Idikula George, Jayashree Kirloskar, Agnes Kramer, E. V. Mackay, G. M. J. Mascarenhas, A. F. Masson, R. W. D. Middleton, R. R. Munro; T. D. Ness, Robert Nikhwa, Ramachandra Pararajasegaram, R. B. J. Peiris, E. R. Price, Tahir Abdel Rahman, Abdur Rashid, Royston Reed-Davis, Sunil Kumar Sarkar, Sohandal Sharma, Hiran Sirikantha Kirth, Singha, Peter Stemmler, David Tanne, W. A. Lisle Thompson, G. M. Thomson, W. G. Walker, G. A. Wall, T. E. C. Williamsz.

### Child Psychiatry in Glasgow

The opening of a new department of child psychiatry (the third of its kind to be established in Scotland) is described in the *Glasgow Herald* of Dec. 16. Associated with the Royal Hospital for Sick Children, it is under the direction of Dr. Frederick Stone, and the permanent staff will include a psychiatrist, a psychiatric social worker, and a child therapist. Its special concern will be emotional health and development in childhood and adolescence, and it will provide a specialist service for diagnosis and treatment. Plans are being made for research and teaching, in coöperation with the departments of child health and psychological medicine in Glasgow University.

### King Edward's Hospital Fund for London

The Fund has received a further instalment of £50,000 from the Nuffield Trust for the Special Areas. In founding this Trust, Lord Nuffield provided that any sums available by way of repayment of loans or otherwise from his trust for the special areas should pass to King Edward's Hospital Fund. In all £1,650,000 has now been received.

### Scientific Film Association

A meeting arranged by the medical committee of this association is to be held on Tuesday, Jan. 17, at 6.30 P.M., at the Mezzanine Cinema, Shell-Mex House, Strand, London, W.C.2, when Dr. Robert Ollerenshaw will discuss the use and abuse of film in medical illustration.

### Common Cold Research Unit

This unit is asking for 600 volunteers during 1956 so that there may be no hold-up in the work. They are anxious to enroll as soon as possible 100 volunteers for the trials from the middle of January till the middle of March. Comfortable living quarters are provided for volunteers. Fares to and from Salisbury are paid up to a maximum of £3, and 3*s.* a day pocket-money is allowed. Volunteers should be between 18 and 45 years of age and in normal health. Further information may be had from the medical director of the unit, Harvard Hospital, Salisbury.

---

CORRIGENDUM : *Rowton Houses.*—In one of the references to Rowton Houses that have recently appeared in our columns (Sept. 17, p. 572), they were described as lodging-houses. This was incorrect. From 1899 onwards legal rulings have established that Rowton Houses do not belong to this category but are hotels or hostels for working-class people.

## Diary of the Week

JAN. 1 TO 7

### Monday, 2nd

DENTAL AND MEDICAL SOCIETY FOR THE STUDY OF HYPNOSIS
8 P.M. (11, Chandos Street, W.1.) Dr. A. A. Mason : Treatment of Oral Disorders by Hypnosis.

### Tuesday, 3rd

ROYAL ARMY MEDICAL COLLEGE, Millbank, S.W.1
5 P.M. Sir William MacArthur : Mediæval Leprosy in the British Island—What Was It ?

INSTITUTE OF DERMATOLOGY, Lisle Street, W.C.2
5.30 P.M. Dr. P. D. Samman : Tuberculosis Cutis.

### Wednesday, 4th

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1
8 P.M. *Surgery.* Dr. R. L. Holt, Mr. W. M. Capper, Prof. A. G. R. Lowdon : Surgical Management of Uncomplicated Duodenal Ulcer.

INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. J. O. Oliver : Mycobacteria in Skin Diseases.

### Thursday, 5th

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, London, W.C.2
5 P.M. Prof. Arnold Sorsby : Some Dominantly Inherited Central Fundus Lesions.

ROYAL SOCIETY OF MEDICINE
8 P.M. *Neurology.* Dr. R. S. Allison, Dr. P. D. Bedford, Prof. A. Meyer : Clinical Consequences of Cerebral Anoxia.

### Friday, 6th

UNIVERSITY OF LONDON
5.15 P.M. (London School of Hygiene and Tropical Medicine, Keppel Street, W.C.1.) Prof. C. De Duve (Louvain) : Intracellular Distribution Patterns of Enzymes. (First of two lectures.)

ROYAL SOCIETY OF MEDICINE
5.30 P.M. *Anæsthetics.* Dr. A. A. Mason : Hypnosis.

INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. G. B. Dowling : Skin Tuberculosis and Sarcoidosis.

ROYAL MEDICO-CHIRURGICAL SOCIETY OF GLASGOW
8.30 P.M. (Royal Faculty of Physicians and Surgeons of Glasgow, 242, St. Vincent Street.) Prof. Graham Bull : Treatment of Disturbances in Body Water and Electrolytes.

## Appointments

GILLIGAN, M. S., M.B. Belf., F.R.C.S.I. : surgeon, Louth county council.

HELLIWELL, PHILIP, M.B. Edin., F.F.A.R.C.S., D.A. : consultant anæsthetist, St. Peter's, St. Paul's, and St. Philip's Hospitals, London.

HODGSON-JONES, I. S., M.D. Camb., M.R.C.P. : consultant dermatologist, Northampton and Kettering areas.

WILLIAMS, W. R., M.B. Wales, D.T.M. & H., D.P.H. : asst. M.O.H. and school M.O., Merionethshire.

**Appointed Factory Doctors :**

CURRAN, D. V., L.R.C.P.E. : Shipley, Yorks.

SHELDON, K. M. M., M.B. Camb. : Bradford East, Yorks.

TURNER, R. E. S., M.R.C.S. : Bracknell, Berks.